STUDY ON SERUM MAGNESIUM LEVEL IN PATIENT S WITH TYPE2 DIABETES AND ITS CORRELATION WITH DIABETIC RETINOPATHY AND NEPHROPATHY"

Dissertation submitted to

THE TAMILNADU DR.M.G.R.MEDICAL UNIVERSITY

in partial fulfillment of the regulations

for the award of the degree of

M.D. BRANCH – I

GENERAL MEDICINE

CHENGALPATTU MEDICAL COLLEGE

THE TAMILNADU DR.M.G.R.MEDICAL UNIVERSITY

CHENNAI, INDIA.

APRIL 2015

CERTIFICATE

Certified that this dissertation entitled "**STUDY ON SERUM MAGNESIUM LEVEL IN PATIENT S WITH TYPE2 DIABETES AND ITS CORRELATION WITH DIABETIC RETINOPATHY NEPHROPATHY"** is a bonafide work done by **Dr. K.LAKSHMI,** post graduate student of the Department of General Medicine, Chengalpattu Medical College, Chengalpattu, during the academic year 2012-2015. This work has not previously fomed the basis for the award of any degree.

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DECLARATION

I am **Dr. K. LAKSHMI.**, solemnly declare that the dissertation titled, "**STUDY ON SERUM MAGNESIUM LEVEL IN PATIENTS WITH TYPE2 DIABETES AND ITS CORRELATION WITH DIABETIC RETINOPATHY AND NEPHROPATHY "** is a bonafide work done by me at Chengalpattu MedicalCollege during 2012-2015 under the guidance and supervision of **Prof. Dr.G.RAJAN.M.D.,** Professor,Department of General Medicine, Chengalpattu Medical College, Chengalpattu. The dissertation submitted to The Tamilnadu Dr. M.G.R. Medical University towards partial fulfillment of requirement for the award of

M.D. (GeneralMedicine)

Place: Chengalpattu **(Dr.K.LAKSHMI.)**

Date :

SPECIAL ACKNOWLEDGEMENT

I gratefully acknowledge and sincerely thank

Prof. DR.RAJA BILLY GRAHAM M.S.,

DEAN

CHENGALPATTU MEDICAL COLLEGE AND HOSPITAL,

CHENGALPATTU.

For granting me permission to utilize the resources of this

institution for my study.

ACKNOWLEDGEMENT

I would like to take this opportunity to express my deep sense of gratitude towards **Dr.G RAJAN.M.D.,** Professor, Department of Medicine, Chengalpattu Medical College, Chengalpattu for his valuable guidance, constant encouragement, and expert suggestions, in spite of his busy schedule, which was most crucial in overcoming various difficulties. I will remain thankful for his guidance, inspiration and constant support.

I am extremely grateful to **Dr.K.Srinivasagalu. M.D.**, Professor and Head of the Department of General Medicine, Chengalpattu Medical College, Chengalpattu for his supervision and keen interest in academic activities.

I am thankful to **Dr.R.Kulothungan.M.D., Dr.R.Muthuselvan.M.D. Dr.S.Mohan RaO M.D Dr.Rajalakshmi.M.D. ,** Professors of Medicine for their guidance and timely help.

I would sincerely thank **Dr.S.Jayalakshmi.M.D.,DM. (Nephrology**), for her valuable guidance and support given during my study.

I am indebted to **Dr.Senthil kumar M.D.,DM (Gastroenterology)** **Dr.E.Velmariappan. M.D., Dr.K.Kamatchi.M.D.,** Assistant Professors of Medicine for their guidance and help given during my course and thesis work. I am extremely thankful to my friend, junior and colleagues for their untiring support.

I thank all others who have assisted me in some form or other in preparation of my thesis.

I would like to thank my parents, in-laws, husband, children (Dharani and Thiyagarajan) and my brother who constantly encouraged me and gave moral support.

Last but not the least; I am grateful to all those patients who were the subjects for this study, without whose co-operation this work would not have been possible.

I bow my head in respect before God Almighty.

Date: **Signature of the Candidate:**

Place: Chengalpattu **Name:**

LIST OF ABBREVATIONS

Ca:	Calcium
CKD:	Chronic Kidney Disease
Cr:	Creatinine
DM:	Diabetes Mellitus
ESRD:	End Stage Renal Disease
FBS:	Fasting Blood Sugar
GDM:	Gestational Diabetes Mellitus
GLU:	Glucose
GLUT:	Glucose Transporter
GTT:	Glucose Tolerance Test
HbA1C:	Glycosylated Heamoglobin
IDDM:	Insulin Dependent Diabetes Mellitus
IFG:	Impaired Fasting Glucose
IGT:	Impairted Glucose Tolerance
K:	Potassium
Mg:	Magnesium
Na:	Sodium
NIDDM:	Non Insulin Dependent Diabetes Mellitus
OGTT:	Oral Glucose Tolerance Test
PPBS:	Post Prandial Blood Sugar
SHT:	Systemic Hyper Tension
Type1DM:	Type two Diabetes Mellitus
Type1DM:	Type one Diabetes Mellitus
Ur:	Urea

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KEY TO MASTER CHART

Mg – Magnesium

DOI – Duration of Illness

BMI – Body Mass Index

NS – Non-Sedentary

S – Sedentary

Ht – Height

Wt – Weight

Kg – Kilogram

FBS – Fasting Blood Sugar

Ur – Urea

Cr – Creatinine

LP – Lipid Profile

NPDR – Non-Proliferative Diabetic Retinopathy

PDR – Proliferative Diabetic Retinopathy

ECG – Electro Cardio Graph

F – Female

M – Male

DATA ON SERUM MAGNESIUM LEVEL IN TYPE 2 DIABETES AND CORREALTION WITH DIABETIC RETINOPATHY AND NEPHROPATHY

Sl No	Name	Age	Sex	Occu	IP/ OP	DOI	Drugs	Wt (kg)	Ht (m)	BMI	SBP	DBP	FBS	HbA1C	S.Mg	U-Pro	Urea	S.C	LP	NPDR	PR
1	THANGAM	51	F	S	OP	5	OHA	45	1.39	23.29	126	82	141	8	1.6	<300	36	1	N	N	Nil
2	THAYEE	58	F	S	OP	6	OHA	56	1.55	23.31	130	92	136	7	1.6	>300	35	1.1	HL	N	NIL
3	SUSEELA	49	F	NS	OP	3	OHA	78	1.58	31.24	140	80	128	6.5	1.7	<300	35	1	N	N	NIL
4	MEENA	43	F	NS	OP	1	OHA	64	1.62	24.39	126	84	118	6	1.8	<300	28	1.2	HL	N	NIL
5	PANJALI	60	F	S	OP	10	OHA	65	1.57	26.37	156	90	130	8	1.6	>300	36	1.2	HL	P	NIL
6	RANI	57	F	S	OP	9	OHA	75	1.52	32.46	138	90	142	9	1.6	<300	34	1.2	HL	P	NIL
7	KANNAN	65	M	S	OP	8	OHA	76	1.64	29.74	150	100	136	9	1.5	>300	40	1.8	HL	N	NIL
8	GOPAL	65	M	NS	OP	10	OHA+INJ	76	1.58	32.89	140	92	126	7	1.6	<300	36	1	HL	P	NIL
9	JAYARAM	69	M	S	OP	6	OHA	80	1.64	10.02	140	90	132	8	1.6	<300	28	1.1	HL	N	NIL
10	GANGA	61	F	S	OP	5	OHA	65	1.42	32.23	140	90	128	10	1.6	<300	36	1.2	HL	N	NIL
11	AMUDHA	50	F	NS	OP	3	OHA	61	1.6	23.82	130	90	116	7	1.7	<300	36	1.2	N	N	NIL
12	SUNDHARI	74	F	S	OP	12	OHA	60	1.63	22.58	140	90	122	7	1.9	<300	32	1.2	N	N	NIL
13	VIJAYA	42	F	NS	OP	2	OHA	75	1.64	27.81	130	80	126	7	1.8	<300	36	1	N	N	NIL
14	BHAI	45	M	NS	OP	3	OHA	95	1.71	32.49	140	90	132	8	1.8	<300	36	1.2	HL	N	NIL
15	CHANDRA	39	F	NS	OP	1	OHA	50	1.52	21.64	130	80	120	6.5	2	<300	32	1.1	N	N	NIL
16	THAMBI	61	M	S	OP	8	OHA	59	1.65	25.71	126	92	126	9	1.7	<300	36	1	N	P	NIL
17	SURYA	55	F	NS	IP	6	OHA	65	1.7	26.1	122	86	135	10	1.5	>300	36	1.2	N	N	NIL
18	BANU	59	F	NS	OP	8	OHA	67	1.49	30.17	130	82	140	11	1.6	>300	38	1.4	N	N	NIL
19	DURAI	64	M	NS	OP	10	OHA	65	1.42	32.25	140	90	130	12	1.4	>300	36	1.2	HL	N	NIL
20	MANI	52	M	NS	OP	6	OHA	79	1.72	27.33	140	90	136	10.5	1.6	<300	35	1	N	N	NIL
21	RAJENDREN	58	M	NS	OP	8	OHA	62	1.58	24.83	138	92	219	10	1.7	<300	36	1.2	N	N	NIL
22	CHELLAM	75	M	S	OP	10	OHA	56	1.62	21.21	150	90	225	9	1.6	>300	38	1.2	N	P	NIL
23	JANAKI	54	F	NS	OP	4	OHA	66	1.5	29.33	152	90	223	11	1.6	>300	38	1.2	N	P	NIL
24	RUBY	60	F	NS	OP	10	OHA	62	1.6	24.21	100	80	98	6	1.9	<300	32	0.9	N	N	NIL
25	CHANDRA	67	F	NS	OP	6	OHA	68	1.7	28.52	128	90	83	6	1.6	<300	30	1	N	N	NIL
26	MANO	38	M	NS	OP	1	OHA	86	1.65	31.59	130	80	240	9	1.6	<300	29	1.2	N	N	NIL
27	RAJU	64	M	NS	OP	6	OHA	72	1.78	26.37	150	90	180	10	1.6	>300	40	1	N	N	NIL
28	PAKARI	59	M	S	OP	5	OHA	78	1.65	28	150	90	250	11	1.5	<300	42	2.1	N	P	NIL
29	SAMI	64	M	NS	OP	7	OHA	82	1.68	29	138	86	164	9	1.7	<300	30	1.2	N	N	NIL
30	THIRU	50	M	NS	IP	3	OHA	65	1.69	32	140	90	118	7	1.9	<300	30	1.2	N	N	NIL
31	RAMESH	38	M	NS	OP	3	OHA+INJ	68	1.65	23	120	80	148	10	1.5	>300	40	2.5	N	P	NIL

32	PANDU	42	M	NS	OP	5	OHA+INJ	70	1.78	22	120	80	98	6.5	1.8	<300	32	1	N	N	NIL
33	PAVUNU	67	F	S	OP	5	OHA	68	1.53	29.5	140	90	145	11	1.6	>300	36	1.1	N	N	NIL
34	BEEBEE	58	F	NS	OP	8	OHA+INJ	69	1.55	28.72	138	80	185	9	1.6	>300	36	1.2	N	P	NIL
35	USMAN	63	M	NS	OP	11	OHA	72	1.61	27.78	130	80	165	11	1.7	>300	38	1.2	N	P	NIL
36	LATHA	60	F	NS	OP	9	OHA+INJ	69	1.58	27.65	140	90	163	9	1.7	>300	36	1.1	N	N	NIL
37	RANI	50	M	NS	OP	6	OHA	75	1.65	27.55	120	90	154	9	1.8	<300	32	1	N	N	NIL
38	MANJULA	49	F	NS	OP	3	OHA	64	1.75	20.09	120	80	100	11	1.6	<300	30	1	N	N	NIL
39	RAMAN	61	M	NS	IP	10	OHA	73	1.71	24.96	136	92	168	10	1.7	>300	38	1.2	HL	P	NIL
40	BALA	57	M	NS	OP	6	OHA	75	1.78	23.67	128	96	115	6	1.8	<300	32	1.2	N	N	NIL
41	MOHAN	56	M	NS	OP	6	OHA	75	1.48	34.24	130	80	263	11	1.6	>300	36	1.2	HL	P	NIL
42	KAMALA	45	F	NS	OP	5	OHA	68	1.63	25.59	134	83	111	9	1.8	<300	34	1	HL	N	NIL
43	KASTHURI	48	F	NS	OP	3	OHA	70	1.56	28.76	130	80	144	9	1.7	>300	36	1.6	HL	N	NIL
44	SUMAN	69	M	NS	OP	11	OHA	69	1.56	27.99	110	82	121	8	1.8	<300	32	1.2	N	N	NIL
45	KATTAN	52	M	NS	OP	6	OHA&INJ	78	1.58	34.67	110	78	148	9	1.6	>300	36	1.2	HL	N	NIL
46	PICHAI	70	M	S	OP	10	OHA	70	1.69	24.51	148	82	105	6	1.7	<300	32	1	N	N	NIL
47	NEELA	71	F	S	OP	9	OHA	65	1.55	27.06	136	88	128	7.5	2	<300	36	1	N	P	NIL
48	THULASI	48	F	NS	OP	5	OHA	64	1.67	22.95	140	78	132	8	1.9	<300	34	1.1	N	N	NIL
49	ARUMUGAM	50	M	NS	IP	5	OHA&INJ	76	1.69	26.61	130	82	152	9	1.7	>300	36	1.2	HL	NI	NIL
50	MURUGAN	48	M	NS	OP	4	OHA	85	1.71	29.07	140	94	252	9.5	1.6	<300	35	1.1	HL	P	NIL
51	KRISHNAN	55	M	NS	OP	5	OHA	80	1.75	26.12	132	82	152	10	1.9	<300	33	1	N	N	NIL
52	BABU	38	M	NS	OP	1	OHA	79	1.8	24.38	128	88	150	8.5	1.9	<300	34	1.1	N	N	NIL
53	THAYALAN	39	M	NS	OP	1	OHA	70	1.74	23.12	124	80	126	8	1.7	<300	36	1	N	N	NIL
54	KALA	40	F	NS	OP	4	OHA	64	1.61	24.69	110	86	105	6.5	1.9	<300	34	1.1	N	N	NIL
55	MURTHY	54	M	NS	OP	8	OHA	73	1.78	23.04	112	82	121	7	1.6	>300	30	1.2	N	N	NIL
56	SASIKALA	41	F	NS	OP	1	OHA	65	1.63	24.4	140	90	115	8	2	<300	36	1.1	N	N	NIL
57	MUTHU	58	M	NS	OP	7	OHA	74	1.74	24.1	130	80	110	6	2	<300	35	1	N	N	NIL
58	RAJA	54	M	NS	IP	4	OHA	72	1.69	25.21	140	82	148	10	1.6	>300	40	1.8	HL	P	NIL
59	SELVAM	52	M	NS	OP	3	OHA	83	1.84	24.52	110	82	96	6	2.1	<300	36	1.1	N	N	NIL
60	SHEELA	58	F	NS	OP	8	OHA&INJ	58	1.5	25.78	120	90	92	6	2	<300	34	1	N	N	NIL
61	JAMEELA	52	F	NS	OP	6	OHA	100	1.55	41.62	140	90	223	10	1.6	>300	36	1.2	N	N	NIL
62	RUPA	49	F	NS	OP	9	OHA+INJ	95	1.65	34.89	140	90	245	10	1.6	>300	40	2	HL	P	NIL
63	ELLAMMAL	63	F	S	OP	9	OHA	65	1.51	28.51	140	80	189	10	1.6	>300	36	1	N	N	NIL
64	THIYAGU	70	M	S	OP	10	OHA	67	1.76	21.63	150	90	90	6.5	1.8	<300	28	1.2	N	N	NIL
65	KILLIAMMAL	69	F	S	OP	9	OHA+INJ	64	1.6	25	150	90	98	6	1.8	<300	28	1.2	N	N	NIL
66	NADHU	41	M	NS	OP	6	OHA	72	1.75	23.51	30	80	116	6.7	1.7	<300	32	1	N	N	NIL

67	PUSHA	59	F	NS	OP	6	OHA+INJ	69	1.57	27.99	150	90	320	11	1.5	>300	36	1.2	N	N	NIL
68	MURALI	51	M	NS	OP	5	OHA	69	1.69	24.16	140	90	236	10	1.7	>300	30	0.9	N	P	NIL
69	LAKSHMI	59	F	NS	OP	6	OHA+INJ	69	1.57	27.99	150	90	220	11	1.6	>300	38	1.2	N	P	NIL
70	SUNDHARI	61	F	S	OP	10	OHA	70	1.55	29.14	140	80	200	11	1.6	>300	30	1.7	N	N	NIL
71	MUNIAMMAL	65	F	S	IP	12	OHA	75	1.52	32.46	130	90	187	9	1.6	<300	26	1	N	N	Nil
72	VARADHAN	75	M	S	OP	15	OHA&INJ	69	1.68	24.45	140	90	210	9	1.6	>300	36	1.2	N	NI	NIL
73	SARASU	68	F	NS	OP	10	OHA	65	1.76	20.98	120	86	188	8	1.6	>300	36	1.2	N	P	NIL
74	MANIMEGALAI	67	F	NS	OP	7	OHA	62	1.58	24.84	150	90	200	11	1.5	>300	36	1.2	N	P	NIL
75	URLAMILA	48	F	NS	OP	5	OHA	68	1.6	26.54	140	90	135	7	1.8	<300	30.8	1.2	HL	P	NIL
76	BRINTHA	40	F	NS	OP	2	OHA+INJ	65	1.65	23.88	130	80	98	6	2	<300	32	1	N	N	NIL
77	BANU	39	F	NS	OP	1	OHA	60	1.62	22.86	130	90	90	6.5	2	<300	26	1	N	N	NIL
78	MEERA	45	F	NS	OP	3	OHA	65	1.59	22.79	126	86	101	7	1.7	<300	28	0.8	N	N	NIL
79	JAYATHI	40	F	NS	OP	2	OHA	60	1.63	22.58	128	78	93	6.5	2	<300	30	1	N	N	NIL
80	KAMATCHI	58	F	S	IP	5	OHA	70	1.66	25.4	130	90	98	6	1.6	<300	32	1	N	N	NIL
81	POOGKODI	55	F	NS	OP	3	OHA	65	1.59	25.71	128	78	105	7	2	<300	28	1	N	N	NIL
82	AMMU	45	F	NS	OP	2	OHA	66	1.58	26.44	126	82	110	8	2	<300	27	1	N	N	NIL
83	SURYA	52	M	NS	OP	6	OHA&INJ	68	1.52	29.43	136	88	112	8	1.7	>300	36	1.2	HL	P	NIL
84	VEERAN	72	M	S	OP	10	OHA	65	1.71	22.23	148	88	115	8.5	1.7	<300	37	1.2	N	N	NIL
85	RATHINAM	78	M	S	OP	12	OHA	78	1.65	25.86	146	90	105	7	1.7	<300	36	1.2	N	N	NIL
86	GOMATHI	69	F	S	OP	12	OHA	65	1.54	27.41	150	100	185	10	1.6	>300	36	1.2	N	P	NIL
87	SEETHA	65	F	S	OP	9	OHA	59	1.59	23.34	148	90	122	7	1.8	<300	30	1.2	N	N	NIL
88	MANI	41	M	NS	IP	1	OHA	75	1.72	22.35	120	8	110	77	1.7	<300	34	1	N	N	NIL
89	SRINIVAS	40	M	NS	OP	1	OHA	70	1.65	25.71	116	78	126	8	1.9	>300	32	1	HL	N	NIL
90	MOHAN RAJ	52	M	NS	OP	4	OHA	65	1.66	23.79	126	70	114	7	1.6	<300	32	1	N	N	NIL
91	DHANAM	55	M	NS	OP	5	OHA	56	1.67	20.08	130	80	96	6.5	2	<300	36	1.2	N	N	NIL
92	THIRUPATHI	60	M	NS	OP	6	OHA	58	1.6	23.39	150	90	89	6.6	2	<300	28	1	N	N	NIL
93	ARUL	42	M	NS	OP	3	OHA	65	1.71	25.97	140	80	100	7	1.9	<300	28	0.9	N	N	NIL
94	NARESH	48	M	NS	OP	5	OHA&INJ	70	1.73	27.6	136	80	109	7	1.8	<300	34	0.8	N	N	NIL
95	DILLI RANI	63	F	S	OP	10	OHA	60	1.52	29.22	140	90	96	7	1.6	<300	36	0.7	N	N	NIL
96	SIVAGAMI	65	F	S	OP	10	OHA	65	1.55	26.3	150	100	256	7	1.8	<300	39	1	N	N	NIL
97	ANJALI	67	F	S	IP	10	OHA	64	1.48	25.39	140	96	101	6	1.9	<300	31	1.2	N	N	NIL
98	SURESH	48	M	NS	OP	5	OHA&INJ	64	1.56	26.3	130	80	156	6	2	<300	30	1.1	N	N	NIL
99	MALAR	58	F	NS	OP	8	OHA	65	1.6	25.39	128	86	181	6.4	1.8	<300	28	0.9	N	N	NIL
100	KUMAR	52	M	NS	OP	5	OHA	73	1.68	25.86	148	90	108	6.4	1.9	<300	30	1	N	N	NIL
101	LEELA	55	F	NS	OP	4	OHA	67	1.54	28.25	130	84	121	7	1.7	>300	36		N	N	NIL
102	SHANMUGAM	59	M	NS	OP	7	OHA	72	1.63	27.1	128	80	111	6.5	1.8	<300	32		N	N	NIL
103	RAVI	69	M	S	OP	9	OHA	70	1.64	26.03	140	86	138	9	1.9	<300	34		N	N	NIL
104	MANNU	66	M	NS	OP	7	OHA	67	1.7	23.18	138	90	120	7	2	<300	30		N	N	NIL
105	SIVA	45	M	NS	OP	3	OHA	79	1.71	27.02	140	90	118	7	2	<300	32		N	N	NIL
106	RAMU	56	M	NS	OP	4	OHA	60	1.68	21.26	146	98	100	6.5	1.9	<300	31		N	N	NIL
107	VADAMALAI	69	M	S	OP	11	OHA	69	1.74	22.79	120	82	132	8	1.7	>300	32		HL	P	NIL
108	DHAMU	56	M	NS	IP	3	OHA	73	1.58	29.24	130	80	125	7.5	1.9	<300	34		N	N	NIL

ABSTRACT

TITLE

A cross-sectional study of serum magnesium levels in patients with Type 2 diabetes mellitus admitted in medical wards in Chengalpattu Medical College, Kanchipuram district.

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KEY WORDS:

Magnesium, Diabetes, Diabetic retinopathy, Diabetic neuropathy, Diabetic nephropathy, Hypomagnesemia.

ABSTRACT:

A high prevalence of magnesium deficiency in found in diabetes. Magnesium deficiency has a negative impact on glucose homeostasis and insulin sensitivity in Type 2 diabetic patients as well as on the evolution of complication such as retinopathy, neuropathy, nephropathy and arterial atherosclerosis.

The aim of this study is to estimate the prevalence of hypomagnesemia in patients with type 2 diabetes mellitus and its correlations with micro and macrovascular complications of diabetes – retinopathy, nephropathy, neuropathy and ischemic heart disease.

Patients with type 2 diabetes admitted in Chengalpaattu Medical Hospital, Chengalpattu over a period of one year between 1st September 2013 to 30th September 2014 formed the study population. The sample size was 100 patients.

The study revealed that prevalence of hypomagnesemia in study subjects was 31%. Sex, age and duration of diabetes were not significant predictors of serum magnesium. Significant association was found between hypomagnesemia and diabetic retinopathy. Significant correlations were found neither with other diabetic microangiopathies nor with comorbitities such as ischemic heart disease and hypertension.

Low serum magnesium concentrations are common in type2 diabetics. Magnesium deficiency is conclusively associated with diabetic retinopathy.

STUDY ON SERUM MAGNESIUM LEVEL IN PATIENTS WITH TYPE2 DIABETES AND ITS CORRELATION WITH DIABETICRETINOPATHY AND NEPHROPATHY

INTRODUCTION:

Diabetes melitus, commonly called as diabetes mellitus, is a group of metabolic disorder of chronic duration in which the person have increase blood glucose (blood sugar), either fasting and/or postprandialiy. It caused by either insulin secretion is not sufficient or the body's cells do not respond properly to insulin, or both. It is one of the cause for leading mortality mortality in developing countries.

The chronic state hyperglycemia leads term damage, dysfunction and failure various system of our body particularly the eyes, kidneys, nerves, heart and blood vessels. Most of people suffering from diabetes fall into two major categories, IDDM *or type 1 DM:* those having minimal or no endogenous secretion of insulin.. *Type 2 or NIDDM:* endogenous insulin secretion capacity is retained but they may have either resistance to insulin action and an inadequate compensatory insulin secretion response. There is increasing incidence of among young people, reproductive age group due to various factor. The risk of developing complication is more and growing among the patients with type2 diabetes mellitus .The disease has become a major public health issue causing huge economic loss in developing and well developed nation.

Impairment of insulin secretion and defects in insulin action can present frequently in the same patient. Several vitamins and minerals act as cofactors in the enzyme reaction regulated by insulin. Deficiencies of certain vitamins and minerals such as potassium, magnesium, zinc and chromium may increase carbohydrate intolerance. Of these, the need for potassium or magnesium replacement is relatively easy to detect based on low serum levels.

Magnesium act as a cofactor in both glucose transport mechanism of the cell membranes and for various intracellular enzymes involved in carbohydrate oxidation. The concentrations of magnesium in serum of healthy people are remarkably constant, whereas 25-39% of diabetics have low concentrations of serum magnesium. The reasons for magnesium deficiency in diabetes may. include increased urinary excretion, lower level of intake , or decreased absorption of magnesium compared to healthy individuals. Magnesium depletion has a negative impact on glucose homeostasis and insulin sensitivity in patients with type 2 diabetes, it has reported that people with diabetes are often obese and their dietary intake of magnesium level was low. It may also due to increased urinary loss see normally in diabetic people involved in the evolution of complications such as retinopathy, arterial atherosclerosis[11] and nephropathy. Moreover, low serum magnesium is a strong self regulating predictor in the development of type 2 diabetes. The present study was undertaken with an aim to estimate prevalence of hypomagnesaemia in patients with type 2 DM and to correlate the serum magnesium concentrations with

micro and macro vascular complications of diabetes-retinopathy, nephropathy and ischemic heart disease and autonomic neuropathy.

OBJECTIVES

This study is aimed at,

1.Estimating the serum magnesium concentrations in patients with Type 2 Diabetes mellitus.

2.Correlating serum magnesium concentrations with complication like diabetic retinopathyand diabetic nephropathy.

3.Correlation serum level magnesium level with blood sugar level

REVIEW OF LITERATURE

DIABETES MELLITUS

It comprises a group of metabolic disorders that share the common feature of increased blood sugar level. Several different types are present and are caused by a interaction of genetics and environmental factors Excessive intake of high calorie, food, sedentary life style and obesity all these increase the risk of diabetes. The word diabetes derived from Greek word meaning to pass through or siphon meaning excessive urination associated with the disease and mellitus means like honey like reflecting sweet smell associated with urination. Increase resistance of insulin to peripheral tissue, defective insulin secretion in response to glucose and glucose over production are three important feature in the development of the disease. It is the leading cause of morbidity and mortality in the future.

HISTORICAL ASPECTS

This disease was first recognized in ancient times, but its history has been evolved over times and is characterized by numerous cycles of discovery, neglect and rediscovery. Its history can be divided into four major periods that reflect different phases in the understanding and management of the disease.

The ‘ANCIENT’ period witnessed the first clinical descriptions of diabetes and complications.

1. From 1600 to 1800 years it has been termed the ‘DIAGNOSTIC’ period, as this disorder was then considered as a separate entity.

2. The middle and late 19th century may be regarded as the first ‘EXPERIMENTAL’ period, characterized by gluco-regulatory role of pancreas has become clear and the disturbances in biochemical diabetes were initially established.

3. The 20th century has seen a dramatic increase in knowledge and awareness about diabetes. Finally, the discovery of insulin in 1921-22 has had profound scientific, clinical and social consequences.

Some key developments in scientific and clinical understanding of diabetes may be summarized as follows:

- Ancient Egyptian papyrus described Polyuric states, clinically resembles diabetes mellitus and discovered by George Ebers as early as 1550 BC.
- Indian physicians observed sweetness of diabetic urine in the 5th and 6th century AD by the (Sushruta and Charaka) and Thomas Willis. in the 17th century.
- John Rollo was first used the term ‘Diabetes mellitus’ meaning honey taste of urine, in the late 1800.
- Matthew Dobson In 1776 postulated that diabetes was a systemic

condition rather than a disorder function in kidneys.

- During the mid to late 19th century, Claude Bernard has stated that liver store the glucose as glycogen and causes hyperglycemia.
- Oskar Minkowski and Josef Von Mering discovered in 1889, that total pancreatectomy causes diabetes in animal.
- During 1869,Paul Langerhans, a medical student freo Berlin- some tissue clumps scattered throughout the pancreases which was later known as islets of Langerhans.
- Edouard Lagussee pointed out that they might produce secretions having the role of regulation in digestion.
- Nicolas Paulesco and George Zuelzer extracted the impure hypoglycemic extract from the pancreas.
- In 1921,Frederick G. Banting, Charles H. Best, James B. Collip and J.J.R. Macleod discovered first Insulin at the University of Toronto.
- In January 1922, insulin was separated from pancreas and experimented that it has the power to lower blood glucose levels in pancreatectomised dogs. Later tested in a human diabetic (Leonard Thompson).

Some of the significant advances in understanding the diabetes and metabolism are :

- Elucidation insulin's three dimensional structure by Dorothy Hodgkin in 1969 and sequencing of insulin by Frederick Sanger in 1955.
- The measurement of insulin concentration using the first radio

immunoassay, by Solomon Berson and Rosalyn Yalow in 1959.

- Separation of proinsulin by Donald Steiner's group in Recognition and classification of specific insulin.

Major achievements in diabetes management is

- The development of long acting insulin preparations.
- Examination and validation of sulfonylureas.
- Use of biguanide (as a first therapeutic measure since 1957.
- Introduction strips suitable for self monitoring blood glucose in the late 1970's.
- Strict glycemic control could slow or prevent the development of diabetic microvascular complications.
- World diabetes day is being celebrated.

every year on 14th November since 1991. This day marks birthday of in 2007. The colour indicates the sky that unites all nations.

The circle indicates the unity of the global diabetes community.

Figure1: Symbol of World Diabetes day

❖ Slogan for this year is “Diabetes: protects our future” The key message are

- **Easy choice to make healthy food**
- **Right choice for healthy eating**
- **Healthy eating starts with breakfast**

Table:1.CLASSIFICATION OF DIABETES

Spectrum of glucose homeostasis and diabetes mellitus

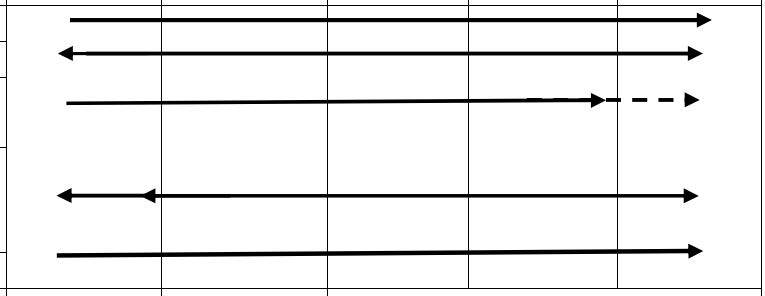
Types of Diabetes	Normal tolerance glucose	Hyperglycemia			
		Impaired fasting glucose or impaired glucose tolerance	Diabetes mellitus		
			Not insulin required	Insulin required for control	Insulin required for survival
Type 1					
Type 2					
Other specific ypes					
Gestational diabetes					
Time(years)					
FPG(mg/dl)	**<110**	**110-125**	**>126**		
	<140	**140-199**	**>200**		

Table1: Classification of Diabetes

Classification based on etiology

I) Type 1 - caused by absolute insulin deficiency due to β-cell destruction which may be due to idiopathic or immune related.

II) Type 2 diabetes- caused by insulin resistance with relative deficiency in

insulin secretion or defect in insulin secretion.

III Specific types of diabetes

Due to mutation causing genetic defect :

1. MODY-1 due to Transcription factor HNF

2. MODY-2due to glucokinase

3. MODY-3 due to HNF1

4 MODY -4 due to Insulin promoter factor

5 MODY- 5.due to HNF – 1β

6. Neuro D1 (MODY 6)

7. Defect in Mitochondrial DNA

8. Defect in Proinsulin or insulin .

Due to genetic defect :

1.1 Lipodystrophy syndromes.

1.2. Rabson-Mendenhall syndrome

1.3. Type A insulin resistance

1.4. Leprechaunism

Exocrine pancreatic diseases like pancreatectomy pancreatitis, neoplasia, hemochromatosis, cysticfibrosis, fibrocalculous pancreatopathy.

- Diseases of Endocrinesystem – Cushing's syndrome, pheochromocytoma, acromegaly,glucagonoma, somatostatinoma

aldosteronoma and hyperthyroidism.

- Chemical or drug related – Vacor, pentamidine, thyroid hormone, nicotinic acid, beta agonists, phenytoin, steroids diazoxide, thiazides, protease inhibitors and clozapine, α– interferon.
- Infections –, cytomegalovirus ,rubella infection, coxsackie.
- Immune-mediated diabetes – "stiff person"syndrome, anti-insulin receptor antibodies.
- Associated with other genetic syndromes: Laurence-moon-biedl syndrome, Turner syndrome Wolfram syndrome, Down syndrome. Klinefelter syndrome Friedreich ataxia etc

IV) Gestational diabetes mellitus (GDM):

PATHOGENESIS

Type 1- due to deficiency in insulin secretion caused by beta cell destruction by autoimmune process. Interaction of genetic, immunological and environmental factors. The susceptibility gene located in HLA DR3 andDR4 region on chr.6 Islet cell antibodies directing against islet molecule (GAD,insulin) are present, Environmental factor like viruses, drugs and bovine milk protein .70-80% of beta cell to be destroyed for the disease to occur.

Type 2- diabetes mellitus is a heterogeneous group of disorders represented by insulin resistance, decreased insulin secretion increased production of glucose and disorder in the fat metabolism.(increased hepatic

production of lipid and glucose).Insulin resistances syndrome-combination of hyperlipidemia, hypertension and insulin resistance.

Metabolic defects in insulin action and/or secretion give rise to the common feature of hyperglycemia in type 2 diabetes mellitus which are different genetic origin.

IDDM and NIDDM are not in use now-a-days as type2 DM also need insulin for management and control of hyperglycemia so the term NIDDM often causes considerable confusion. Age factor is not a important criteria for the classification. Though type 1 diabetes mellitus develops commonly before the age of 30, the autoimmune beta cell destructive process can be occur at any age. It is estimated that type 1 diabetes mellitus develop much earlier ,before age of 30 which constitute5-10%pooulation,auto immune destruction occur at any age.. Similarly, type 2 diabetes mellitus mostly typically occur in individuals with increasing age. However it can also affect the children, obese adolescents in particular.

TYPE 1 DIABETES MELLITUS

Diabetes with immune mediation (Type 1A)

Accounts for only five to ten percent of those affected with diabetes, arises from abnormality in a cell mediated and humoral system leads to immune destruction of the islets of beta cells, autoantibodies to hormonal

insulin, islet cell auto antibodies, autoantibodies to the tyrosine phosphatases IA-2 and IA-2B, autoantibodies to GAD65. IA2/ICA512, Glutamic acid decarboxylase (GAD65) are some of the markers for the disease showing auto immune activity.

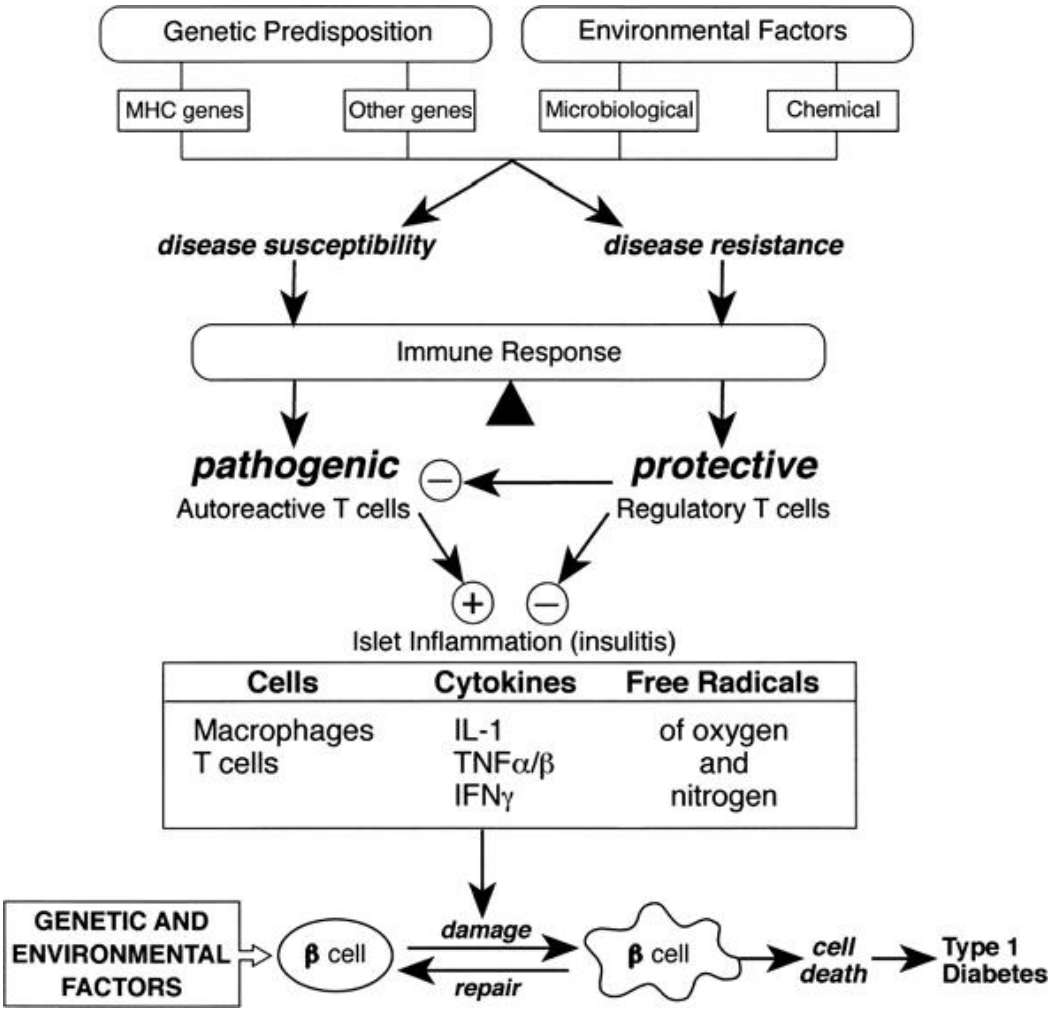


Figure 2 : Factors involved in type 1 Diabetes Mellitus

When fasting hyperglycemia is initially recognized ,one or usually more of these auto antibodies are present in >90%patients. Most affected individual have HLAA1*0301,HLADQB1*0302 andHLADQB1*0201.

In this type of diabetes, rate of β-cell destruction is varied. In young individuals (mainly infants and children) the destructive process and fast manifestation of the disease may be with of clinical features of ketoacidosis and in adults it is slow. In some patients with increased fasting sugar level can go for severe hyperglycemia and / or ketoacidosis in the presence infection and condition like stress. This immune mediated can occur at any age from childhood to adolescence, though it can occur even in old age .They association with other autoimmune disorders such as- Grave's disease, pernicious anemia hashimoto's thyroiditis, vitiligo addison's disease, autoimmune hepatitis, celiac sprue, myasthenia gravis

Type 1B Idiopathic Diabetes

There is no evidence any etological factors or auto immunity But most people suffered from insulinopenia and are prone to ketoacidosis. Mostly common in African or Asian origin ,with type 1 diabetes mellitus. They suffer from episodic ketoacidosis and show evidence of insulin deficiency of varying degree.

Type 2 Diabetes Mellitus

Approximately more than 95% of people with diabetes, belong to this group who usually have relative (rather than absolute) insulin deficiency

and insulin resistance. There may be many different causes to form this diabetes. However specific etiologies are not recognized. Most of the patients with type-2 diabetes mellitus are obese, and obesity itself creates some degree of insulin resistance.

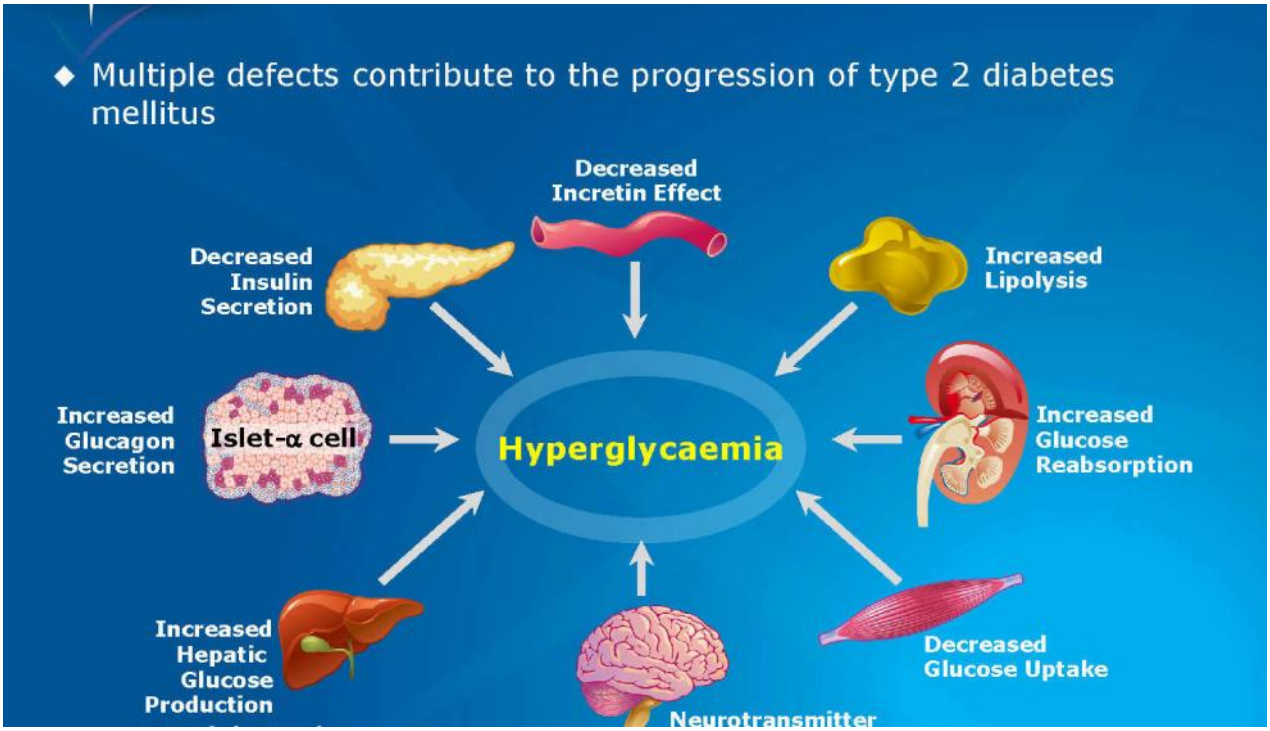


Figure 3 : Factors involved in pathogenesis of Type 2 Diabetes Mellitus.

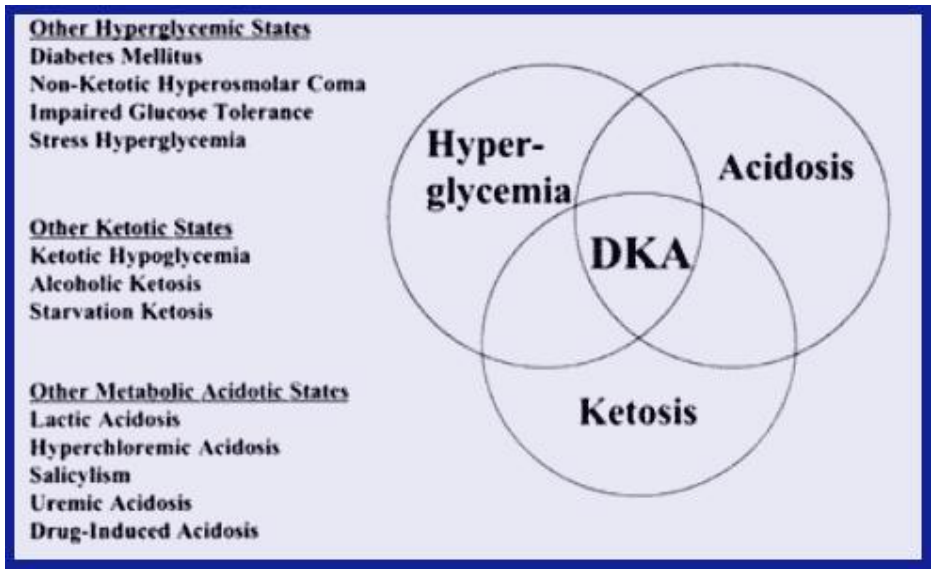


Figure 4 : Interrelationship of Diabetes and its complications

Ketoacidosis rarely occurs spontaneously. Since hyperglycemia develops gradually in this form of diabetes it often goes undiagnosed for many years. Such patients are at increased risk of developing complications.

Complications of diabetes mellitus:

Acute complications:
- Hyperglycemia
- Diabetic ketoacidosis (DKA)
- Hyperosmolar coma
- Hypoglycemia

Chronic complications:
- Macrovascular diseases -Accelerated atherosclerosis
  -Hypertension
  -Hypertriglyceridemia
- Microvascular diseases -Retinopathy
  -Nephropathy
  -Neuropathy
- Other chronic complications-Diabetic foot ulcer
  -Recurrent infections

OTHER SPECIFIC TYPES OF DM

It may be due to specific gnetic defects leads to impaired secretion or action,or mitochondrial or metabolic abnormalities, and other conditions that impair glucose tolerance. Penetrance by autosomal dominant inheritance. MODY is a subtype characterized, impairment insulin secretion and early onset of hyperglycemia.

Pancreatic exocrine disease where the majority of islets (>80%) are destroyed.. Hormones that alienate the action of insulin can also cause diabetes mellitus.IT is often associated with other endocrine disorder like Cushing's disease ,acromegaly etc.

GESTATIONAL DIABETES MELLITUS (GDM)

Diabetes induced by pregnancy because of exaggerated physiological changes occurring in pregnancy or type 2DM unmasked or discovered during pregnancy. It may present approximately in 4% of pregnancies revert to normal glucose tolerance during her postpartum, having a moderate risk of developing the disease later in their life.

Age: women > 25 years old
History of gestational diabetes
Being overweight
Ethnicity (African Americans, Hispanics, and Asians are at greater risk)
Number of previous pregnancies
Sedentary lifestyle
History of smoking
Having polycystic ovarian syndrome

Figure 5: Effects of Gestational Diabetes. Figure 6: Risk factors for GDM

Women with strong family history, given birth to large baby >4kg, having history recurrent fetal loss, persistent glycosuria, obese women or over weight women >15% of non pregnant level weight are some of the risk factor for gestational diabetes. Two types of test are available.

1. 100g glucose with 3 hour GTT.

2. With 75 g glucose and 2 hour GTT. More than 140mg/dl after 2hour of 75 gm glucose considered as gestational diabetes.

Mechanism of insulin resistance:

Insulin resistance as evidenced by decrease in efficiency in insulin action.In elderly obese individual insulin injection has decreased effectiveness. Deficency in both action and secretion of insulin must be present for diabetes to manifest. Fasting insulin concentration is used for assessing insulin resistance.

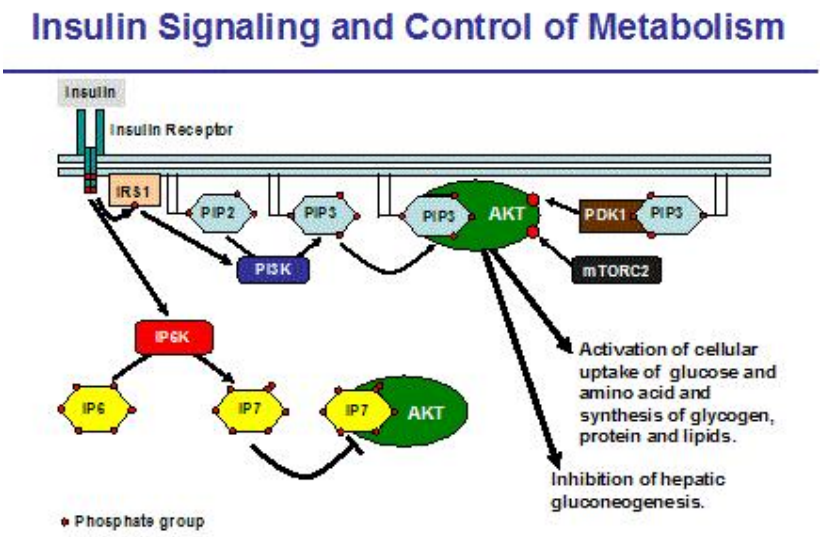


Figure 7: Insulin Signaling and Control of Metabolism.

The musculoskeletal system, liver, fat and adipose tissues are most susceptible to insulin resistance. Hereditary and environmental are also involved in the development of resistance. There are many conditions associated with insulin resistance such as, normally in aging population, puberty, malnutrition, pregnancy and in abnormal conditions like polycystic ovarian syndrome, endocrine disorders like Cushing syndrome, acromegaly, obesity etc.

The Sodium-linked glucose transporters are present in the intestinal system and the kidney are actively involved in the transportation of glucose against a concentration gradient. The other glucose transporters are functioned by facilitated diffusion. GLUT – 1,2,3,4,5 are the five transmembrane proteins

that functions in the similar manner. Of this GLUT-4 is an important glucose transporter present in muscles and adipose tissues. The GLUT-4 is the main insulin-responsive glucose transporter and is located primarily in muscle cells and adipocytes. The post receptor defect in conducting the massage to the insulin receptors is the mechanism for the development of insulin resistance.

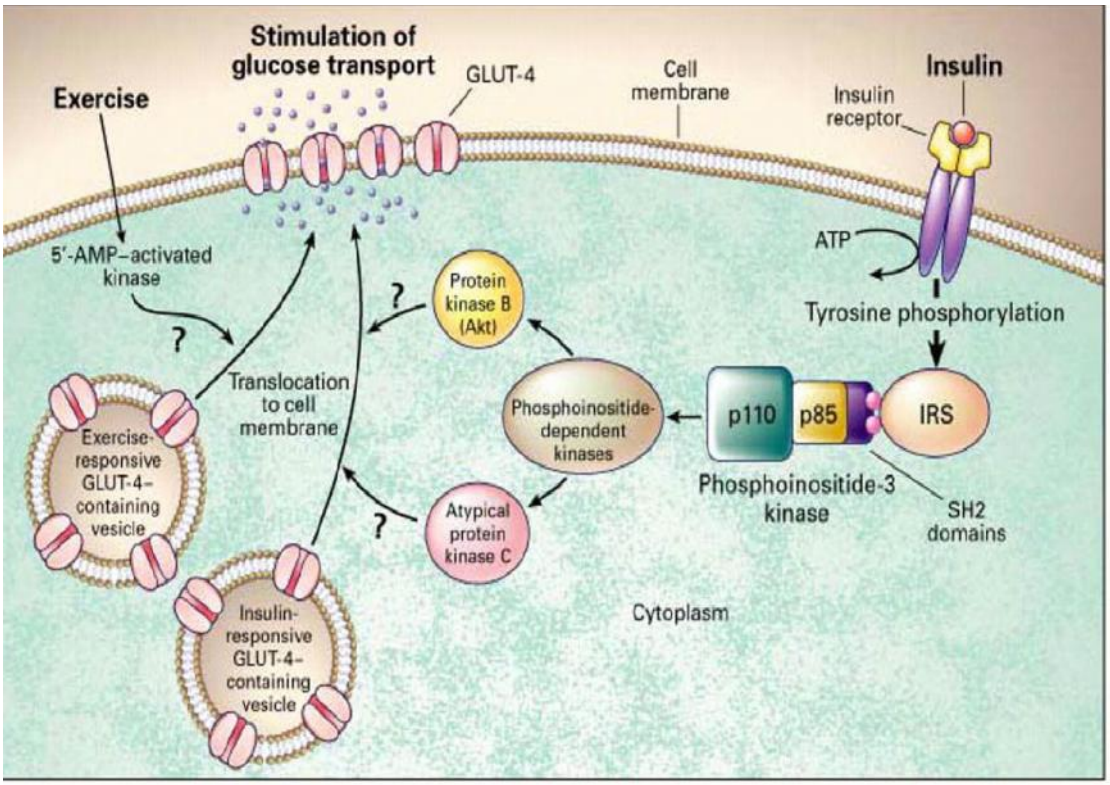


Figure 8 : Mechanism of involving GLUT receptors in insulin action.

In the absence of insulin, GLUT-4 is destroyed within the vesicles. Within the onset of insulin secretion or exercise, GLUT-4 move to the plasma membrane, combine with the vesicles and increase the rate of transport of glucose into the cells. In the absence of insulin stimulation, GLUT-4 is

re-internalized into the storage pools. Insulin acts by phosphorylation of its receptor present in the plasma membrane.

RISK FACTORS FOR THE INSULIN RESISTANCE

The risk factors for the development of insulin resistance include:

1) Lack of physical exercise.

2) Food containing high fat.

3) Baby born with low birth rate.

4) Old-age.

5) Android obesity.

Epidemiology

Type1:Wide geographic variation in the prevalence and incidence is present. Finland has the highest number. globally(0-14years) –approximately 5 laks and annually 76000 children are developing the disease.

Figure 9: Global distribution of Diabetes

Type2: 285 million people are affected by this disorder. Global increase of 6.6 % to 7.8% in last 20 years. China has got highest prevalence around 30%.

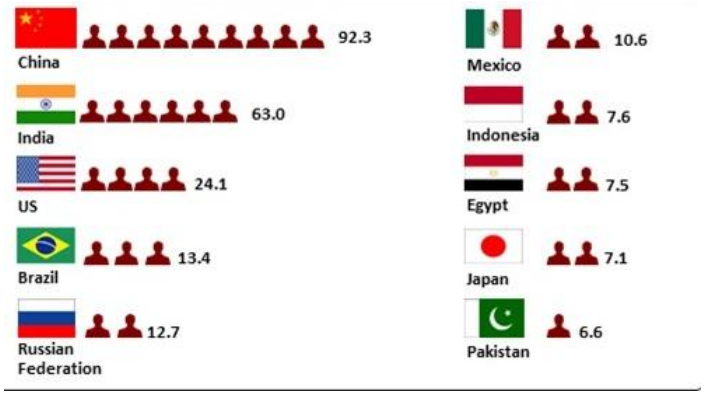


Figure 10: Top 10 countries affected by Diabetes (Millions)

Gestational diabetes: More common in Asian and Indian. Around 70% women with GDM having the chance developing the disease in subsequent pregnancy.

In INDIA: The prevalence increased from 12%to 19% in urban areas and 4%to 9% in rural areas in 2011. Andhra Pradesh and Maharashtra has highest number of cases.

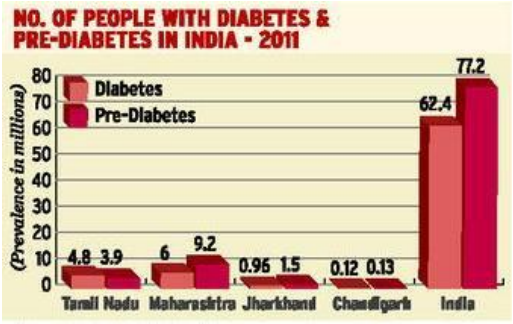


Figure 11: Prevalence of Diabetes and Non-Diabetes in India.

Annual incidence of 18% developing the disease among IGT. Prevalence of developing retinopathy is 27%, overt nepharopathy is about 2.3%,microalbuminuria is 27% peripheral neuropathy-26% and coronary heart disease is 21% among the diabetes.

IMPAIRED GLUCOSE TOLERANCE (IGT) AND IMPAIRED FASTING GLUCOSE (IFG)

10-50% of patients with impaired glucose tolerance develop Type 2 DM over a period of 10 years. Diagnostic criteria for impaired GTT are:

It is defined by two hour oral glucose tolerance test where the plasma glucose is more than 40mm/dl but less than 200 mg.

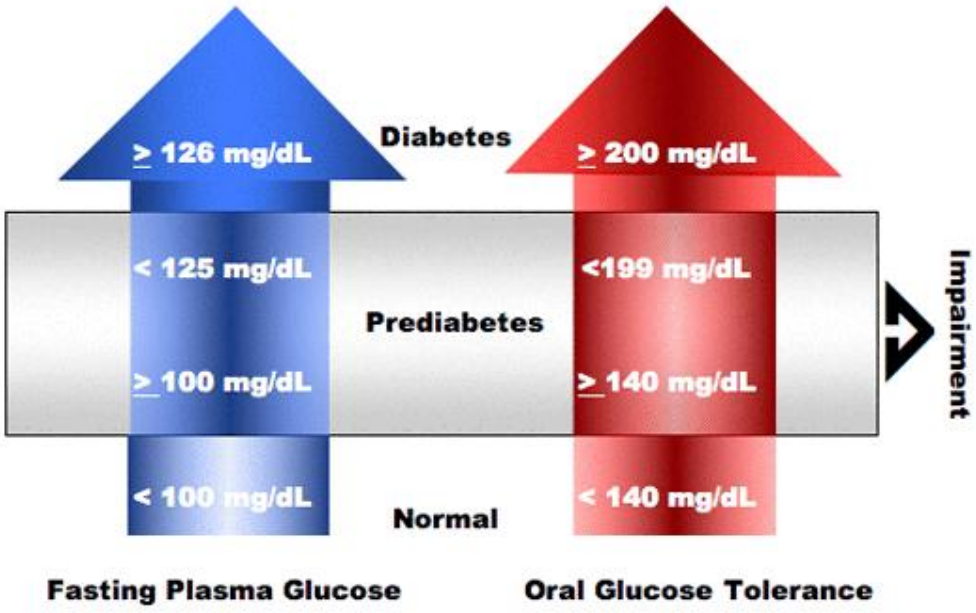


Figure 12: Impaired Glucose Tolerance

Table 1. Re-Examination of the Diagnostic Thresholds for Diabetes and Lesser Degrees of Impaired Glucose Regulation.[20]

Category	FPG	2-hour Postprandial Glucose
Normal	<100 mg/dL (<5.6 mmol/L)	<140 mg/dL (<7.8 mmol/L)
IFG	100–125 mg/dL (5.6–6.9 mmol/L)	—
IGT	—	140–199 mg/dL (7.8–11.1 mmol/L)
Diabetes*	≥126 mg/dL (≥7.0 mmol/L)	≥200 mg/dL (≥11.1 mmol/L)

When both tests are performed, IFG or IGT should be diagnosed only if diabetes is not diagnosed by the other test.

*A diagnosis of diabetes should be confirmed on a separate day.

Impaired fasting glucose is defined by a fasting plasma glucose of 110 mm/dl or greater but <126mm/dl.

Patients with IGT and IFG are also known as having ‘Prediabetes’. and they are prone for micro/macro vascular complications and end up with overt DM Type 2.

They are at risk atherosclerosis. They hence need further evaluation at a later date since they are potential diabetics.

DIAGNOSTIC CRITERIA FOR DIABETES MELLITUS

- Symptoms of diabetes such as frequent hungry, urination, thirst and tiredness and blood glucose concentration 200mg/dl done randomly

Figure13: Common Symptoms of Diabetes Mellitus

- Plasma glucose content >126 mg/dL in the fasting state.
- Plasma glucose >200 mg/dL during OGTT or after two-hour of meal.

- Random means without regard to time.

Table:3

Blood Test Levels for Diagnosis of Diabetes and Prediabetes

	A1C (percent)	Fasting Plasma Glucose (mg/dL)	Oral Glucose Tolerance Test (mg/dL)
Diabetes	6.5 or above	126 or above	200 or above
Prediabetes	5.7 to 6.4	100 to 125	140 to 199
Normal	About 5	99 or below	139 or below

Definitions: mg = milligram, dL = deciliter
For all three tests, within the prediabetes range, the higher the test result, the greater the risk of diabetes.

Table3:Blood Test Levels for Diagnosis of Diabetes and Prediabetes

- Fasting means no intake for not less than 8 hrs since the last meal.
- Diabetes can be diagnosed in three possible, the use of the hemoglobin A1C (HbA1C is not recommended.

SCREENING

Diabetes mostly got unnoticed and diagnosed after the complications had occured. About 1/3th of people with diabetes are still not diagnosed. However,

early diagnosis through screening of asymptomatic individuals demonstrating benefits. But wide spread screening test for T-2 diabetes mellitus using FPG is justified in individuals at high risk.

Risk factors for Type 2 Diabetes Mellitus

- If a parent or sibling of the family is suffering from increased blood sugar.
- The chance of getting diabetes increases with age after 45
- The chance of getting the disease is greater in Hispanics, African-Americans, Native Americans, and Asians. It develops with the Race or ethnic back ground.
- Metabolic syndrome.
- Patient with high lipid profile.

Figure 14: Risk factors for Diabetes Mellitus

- Being overweight as defined by body mass index

- Higher risk of type 2 diabetes for the individual having (BMI) greater than 25.
- Previously identified IFG or IGT
- High blood pressure increases the risk of diabetes development.
- Mother of large birth weight baby.
- Past history of vascular disease.

Recommendations

Diagnosis and evaluation can be carried out in a primary health care system. People with Body Mass Index more than or equal to 25 kg/m^2, must be monitored for every three years beginning at age of 40-45, and if the risk factors are present, testing should be carried out at an early stage.

First the Fasting Blood Sugar is the recommended screening if it is abnormal then Oral Glucose Tolerance test is recommended.

.

An Fasting Blood Sugar more than 126 mg/dl is an indication for re-testing. If FPG level is less than 126 mg/dl then there is a high suspicion for diabetes and OGTT should be performed. A 2hr post load value of more than 200mg/dl is a positive test for diabetes.

The HbA1C remains a valuable tool for monitoring glycemic control for

3-4 months.

STANDARDS OF MEDICAL CARE IN DIABETES

- Medical history of the patient.
- Initial recognition and evaluation.
- Symptoms, outcome of the lab tests, and special examination for the diagnosis.
- Previous HbA1C account.
- Nutritional status, eating habits, growth and development records in the children and adolescents stage.
- Information from previous health records. Current treatment plan of diabetes, including medications, intake of food items and results of glucose monitoring and its use by the patients
- Daily lifestyle habits.
- Watching for complications such as ketoacidosis and hypoglycemia.
- Past and present status of infections especially skin, foot, genitourinary infections and dental.
- History of signs and symptoms and treatment of chronic kidney, eye, nerves, genitourinary, bladder, and gastrointestinal function.
- History of medications for chronic aliment.

- ❖ Searching for atherosclerosis risk.
- ❖ History of endocrine disorders, obesity disorders.
- ❖ History of any psychiatric disorder.
- ❖ Family history and status of diabetes and other endocrine disorders.
- ❖ History of social and environmental factors.
- ❖ History of alcohol and drug abuse.
- ❖ History of sexual misbehavior and contraception.

Physical examination

- ➢ Maturation stage on sex during pubertal period.
- ➢ Anthropometric measurement and comparison.
- ➢ Determination of hypertension, including orthostatic measurements and compare with age-related norms.
- ➢ Fundoscope Examination.
- ➢ Examination Oral, Cardio Vascular system, Abdomine(e.g. for hepatomegaly).
- ➢ Detection of Thyroid disorders.
- ➢ Examination of peripheral pulses.
- ➢ Examination Hand and foot, dermatological and neurological disorders.

- Examination to detect secondary causes of the disease.

Laboratory evaluation

- Determination of HbA1C.
- Testing of liver function.
- Testing of urine for microalbuminuria
  - Analysis of renal function in adults and if proteinuria is present in children
  - Testing of thyroid profile .
  - Cardiovascular examination.
  - Urine- protein, sugar,deposits.

Referrals

- Examination of Eyes,.
- Testing of reproductive age women undergone family planning.
- If MNT needed,
- Dietery management.

**Recommendations Diabetes in Adults **

Table:4.Summary of recommendations for adults with diabetes	
Glycemic control HbA1C Fasting blood glucose Postprandial plasma glucose	 > 7.0% 90 – 130 mg/dl < 180 mg/dl
BP	< 130/80 mmHg
Lipids Low density lipo protein Triglycerides High density lipo protein	 Less than 100 mg/dl (<2.6 mmol/l) lessthan150 mg/dl (<1.7 mmol/l) more than 40 mg/dl (> 1.1 mol/l)

Table4: Summary of recommendation for diabetes in adults.

Key concepts in setting glycemic goals:

- Goal for each and every Individual person.
- special attention to vulnerable age group., pregnant mother , elderly person and children.

  For patients with strict or frequent hypoglycemia Less intensive goals should be indicated .

- Postprandial blood sugar.

Complications

Diabetes has both acute and long term complications.[2]

Acute

- Diabetic ketoacidosis
- Hyperglycemic Hyperosmolar state
- Hypoglycemia

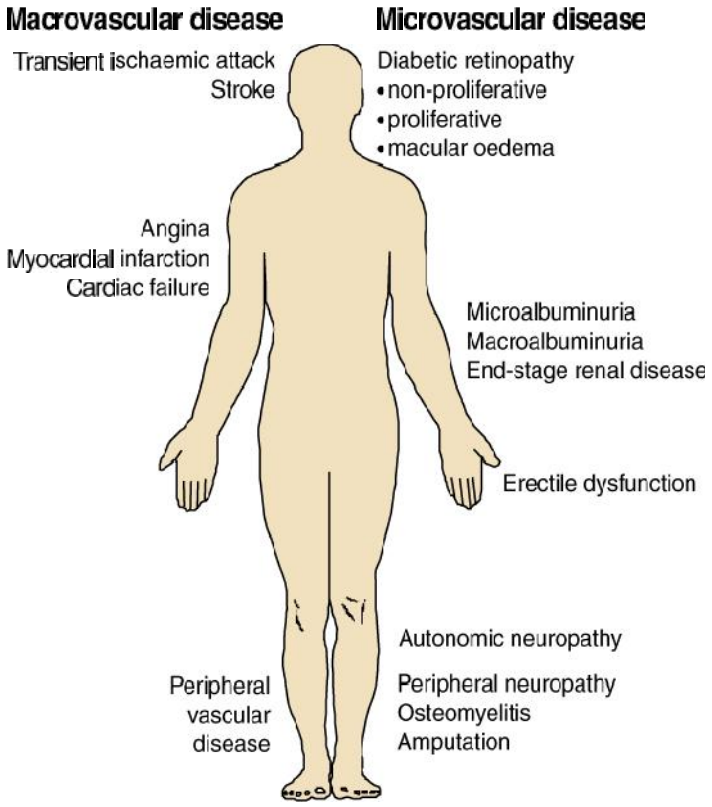


Figure 15: Complications of Diabetes Mellitus

Long term

- Retinopathy

- Neuropathy
- Nephropathy
- Ischemic heart disease
- Cerebrovascular disease
- Peripheral vascular disease
- Hypertension.
- Others

Infections

- UTI
- Tuberculosis
- Candidiasis – oral / volvovaginal
- Mucor mycosis
- Necrotising fasciitis
- Periodontitis
- Duputrens contracture
- Pseudogout

DIABETIC RETINOPATHY :

It is sight threatening chronic micro vasculature complication mostly all patient of diabetes.

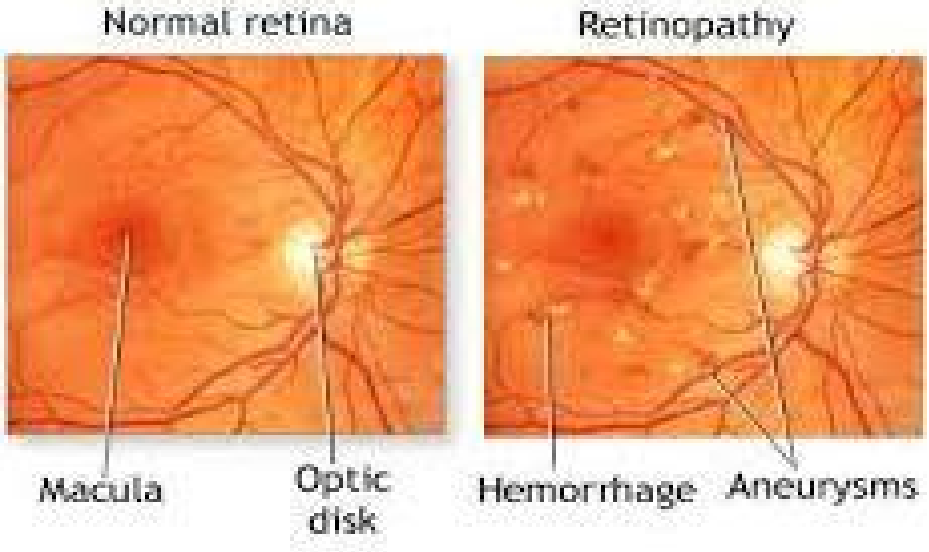


Figure 16: Showing the difference between Normal retina and Retinopathy.

It lead to retinal non perfusion, increased vascular permeability, intra ocular proliferation blood vessels(macular edema)and uncontrolled neo vacularisation (proliferative retinopathy)leads to severe visual loss.

CLASSIFICATION :

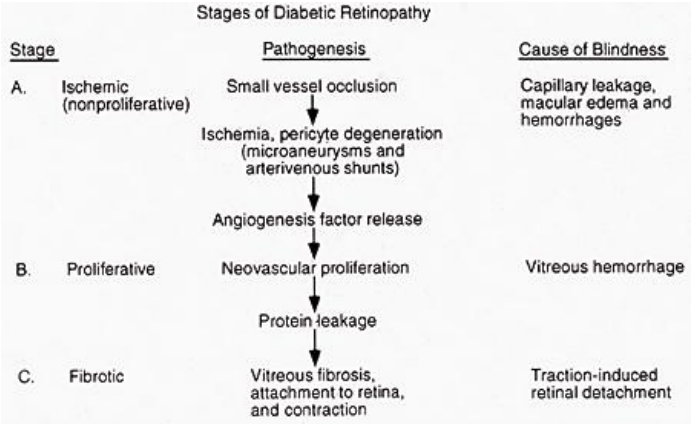


Figure 17 : Flow Chart showing stages of Diabetic Retinopathy

1.No apparent retinopathy.

2. Mild NPDR-micro aneurysms only

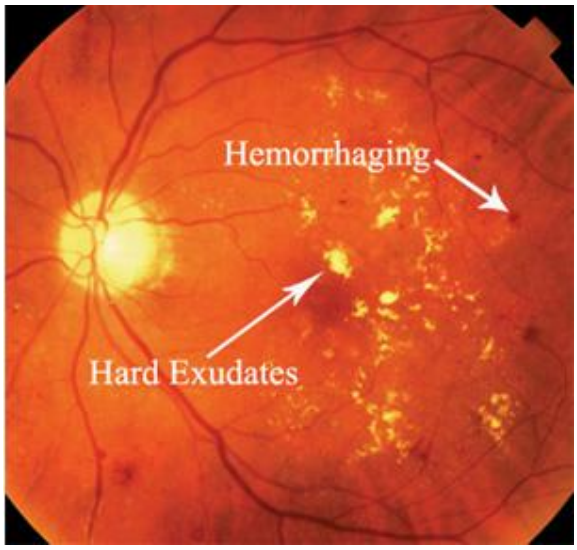
: 

Figure 18: Non-proliferative retinopathy

3.Moderate NPDR-more than micro aneurysms but less than severe NPDR

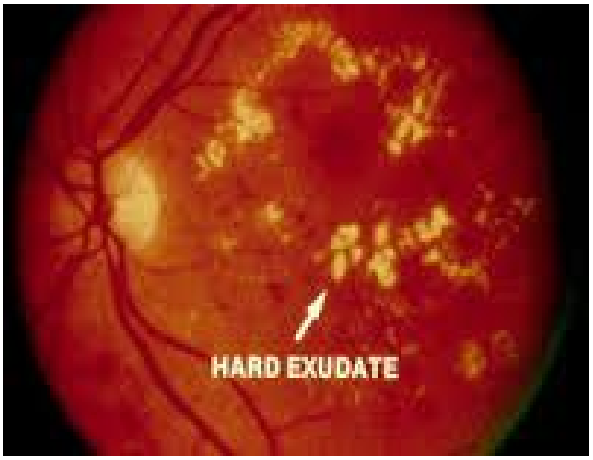


Figure 19: Moderate Non-proliferative retinopathy

4.Severe NPDR->20 intra retinal hemorrhages in each quadrant,venous beading,prominent micro vascular abnormalities and no PDR.

5.PDR-One or more retinal neovascularization,vitreous hemorrhages,pre retinal haemorrhages.

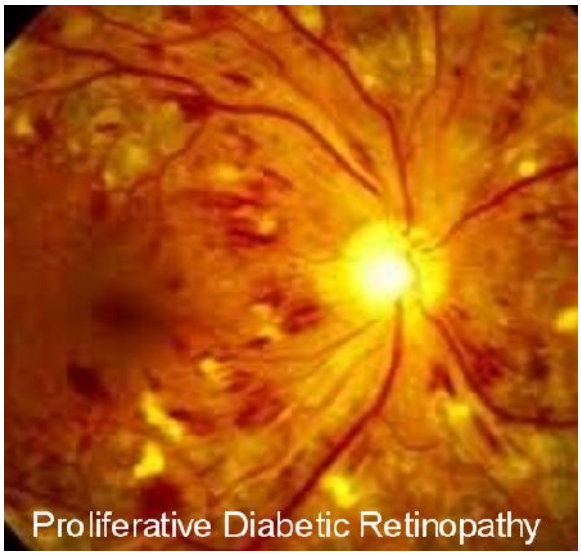


Figure 20: Proliferative Diabetic Retinopathy

Macular edema: classified into two types

1. Not apparent-no retinal thickening or hard exudates in the posterior pole,

2. Apparent- presence of hard exudates,(mild-retinal thickening but distinct from Centre of macula, mod-thickness grows towards the centre, severe-involving whole macula.

Other ocular complication: Mono neuropathies involving 3,4,6 nerves, neo vascular glaucoma, open angle glaucoma, change in the refractive error, cataract bulbar conjunctivitis etc.

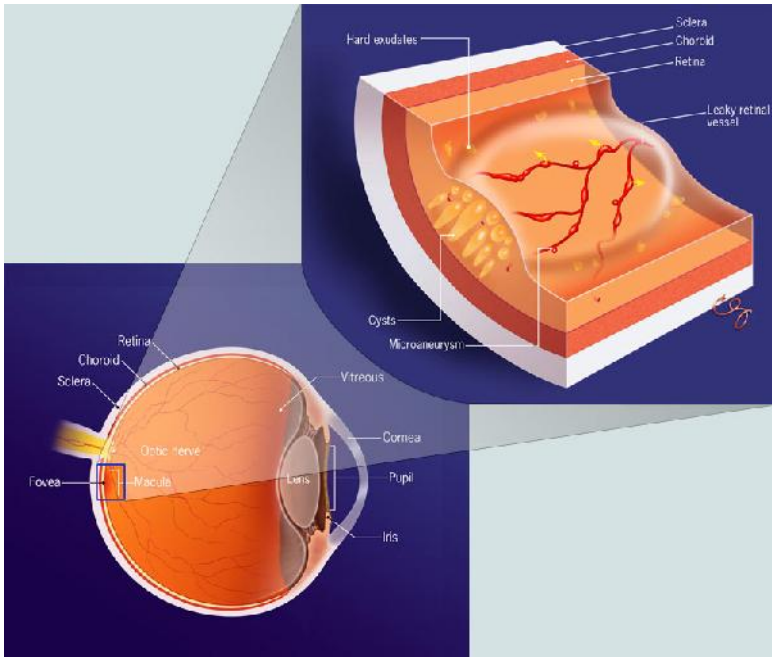


Figure 21: Macular edema

Diabetic retinopathy starts with mild NPDR and progress through moderate and severe NPDR to proliferative diabetic retinopathy. Macular edema can develop at all stages. NPDR generally develops later part of the first decade or early 2nd decade of type – 2 diabetes mellitus. PDR usually develops within 5 years of NPDR. Pregnancy, hypertension, poor glycemic control, and cataract surgery may accelerate these changes. For every percentage reduction of HbA1C (eg. From 8 to 7%), there was a 35% reduction in risk of retinopathy,[19] and tight BP control (to < 150/85 mmHg) results in 34% reduction in progression of retinopathy.

Diabetic Nephropathy

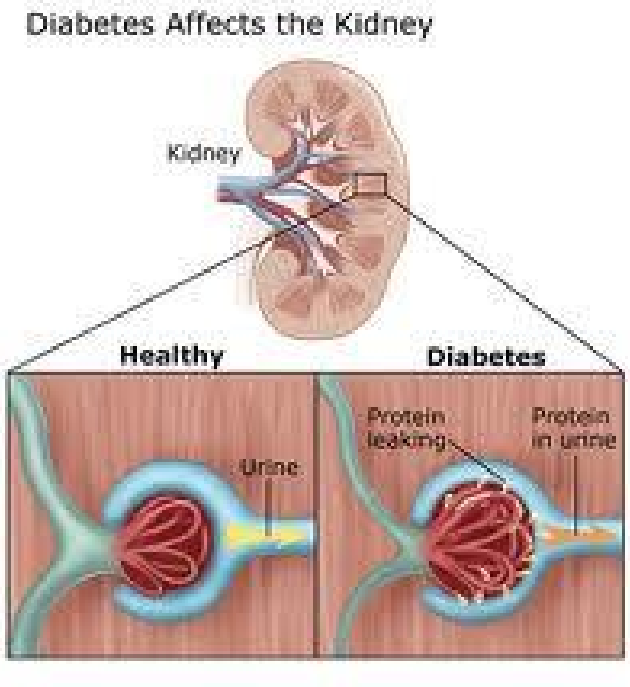


Figure 22: Diabetic Nephropathy

World wide, diabetes is one of the most responsible cause of (ESRD). About 25% of patients with diabetes show evidence of nephropathy, but in type 2 diabetes a smaller proportion of these patient may advanced into end stage renal disease. Due to higher prevalence of type 2 diabetes mellitus, they may constitute over half of patients with nephropathy needing to do dialysis.[1] The diabetic nephropathy progresses from appearance of low but abnormal levels (≥ 30mg to 299 mg/day or 20µg/min) of albumin in urine (microalbuminuria stage) to stage of macroalbuminuria / clinical albuminuria (≥300mg/dl or ≥200µg/min)

to ESRD. Microalbuminuria to macroalbuminuria normally takes 10-15 years. ESRD develops within 10 years in 50% of type 1 diabetic individual with nephropathy and in 20 years by 75%. But in type 2, even after 20 years of overt nephropathy only 20% progress to ESRD.

Screening for Microalbuminuria

A test for the presence of urinary microalbumin should be done for every six month in patients with type 2 diabetes mellitus and after 5 years of disease. In type 1 diabetes mellitus, this repeated annually. It can be performed by three methods.

- Spot estimation protein to creatinine ratio in urine 24 hr Urine collection and estimating of albumin excretion.
- Timed (e.g. 4 hr or overnight) collection.24 hr collection of urine is most reliable.

Table:5Diagnostic values of Albuminuria in Diabetes

condition	spot collection (mg/dl)	24 hrs collection(mg/24hrs)	Timed collection (µg/minute)
Normal	<30	<30	<20

Micro albuminuria	30-299	30-299	20-199
Clinical albuminuria	≥ 300	≥ 300	≥ 200

Table 5: Abnormalities of urine secretion

In addition this, earliest manifestation of nephropathy, marker of greatly increased cardiovascular morbidity and mortality for patients with either form ofdiabetes.

Diabetic Neuropathy

Diabetic neuropathy occurs in fifty percent patint with long standing type 1 or type 2 diabetes mellitus . neuropathy correlates with glycemic status and the duration of disease.

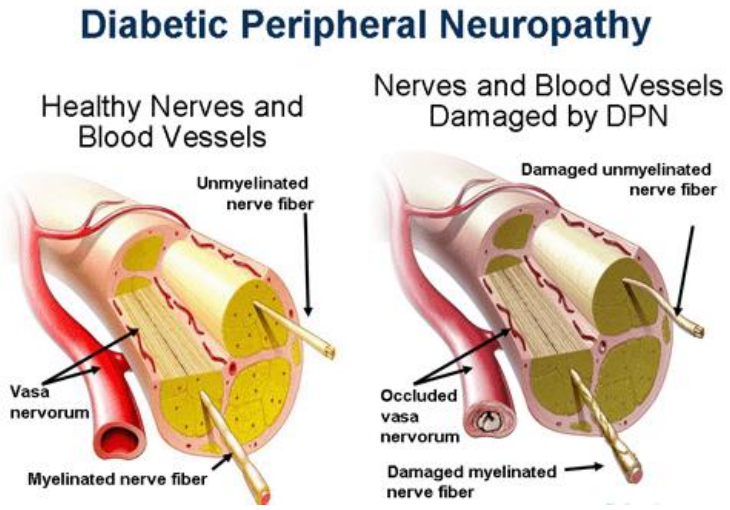


Figure 23: Diabetic Neuropathy

Classification

It envolves both limbs lower more than upper symptoms pain paresthesias, and dysesthesias. Small fibre neuropathy is less common and alpha and C fibre are more involved causing burning or stabbing in nature, more severe at night. Large fibre neuropathy leads to electrical tingling like sensation. The patient may have sense of imbalance with gait instability.

Symmetric

- Distal, primarily sensory polyneuropathy.
- Autonomic neuropathy
- Chronic proximal motor neuropathy

Asymmetric

- Acute or subacute proximal motor neuropathy.
- Cranial mononeuropathy
- Truncal neuropathy
- Entrapment neuropathies

Also classified as follows (Watkin's and Edmond's classification)[21]

1. Progressive Neuropathies

- Chronic sensory motor neuropathy
- Autonomic neuropathy

2. Reversible Neuropathies

- Mononeuropathies
- Proximal motor neuropathy (Amyotrophy)
- Cranial nerve palsies (III,IV,VI)
- Truncal radiculopathies
- Acute painful neuropathies

3.Pressure Palsies

- Carpal tunnel syndrome.

Distal symmetric polyneuropathy : Glove and stocking like sensation in both lower limbs and involves the hands in severe cases. All sensory functions may be affected. Ankle reflex may be reduced or absent and wasting of small and in severe cases large muscle may occur. Most common form of diabetic neuropathy and most frequently represents as distal sensory loss. Hyperesthesia, paresthesia and dysesthesia may also be occur. Painful neuropathies may develop in these patients. Acute (lasting < 12 months) as well as chronic form of painful diabetic neuropathies have been described below.

Individuals with long standing type 1 or type 2 diabetes mellitus may develop autonomic neuropathy. It involves all system including cardiovascular, gastrointestinal, genitourinary and metabolic systems. Resting tachycardia, gastroparesis orthostatic hypotension, hyperhidrosis of upper extremities, bladder emptying abnormalities, and anhidrosis of

lower extremities are features of diabetic autonomic neuropathy.

CARDIOVASCULAR DISEASE IN DIABETES

Incidence cardiovascular disease is increased in individuals with type 1 or type 2 diabetes mellitus. A Study conducted by the Framingham Heart revealed that a marked increase in peripheral arterial disease, coronary artery disease, myocardial infarction, congestive heart failure and sudden death (risk increases from one to five fold) in diabetes mellitus.22 The American Heart Association recently designated type 2 diabetes mellitus as a coronary risk equivalent i.e. they have a similar 10 year risk of MI, as those who have had a prior MI.1 Because of extremely high prevalence of underlying cardiovascular disease in patients with type 2 diabetes mellitus, evidence of atherosclerotic vascular disease should be sought in a diabetic who has symptoms suggestive of cardiac ischemia, peripheral or carotid artery disease, a resting ECG indicative of prior MI, plans to initiate an exercise program, proteinuria or two other cardiac risk factors. (ADA recommendations).[1]

In addition to coronary artery disease, cerebrovascular disease is increased in individuals with diabetes mellitus (three fold increase in stroke). Proof that improved glycemic control reduces cardiovascular complications in diabetes mellitus is lacking.16

Magnesium

Magnesium is the fourth most abundant cation in the body and second most ion in intracellular tissue materials. Magnesium content in an adult human body is 21-28gms (approximately 2000mEq). About 60% of total body magnesium is concentrated in bone and the remainder is in soft tissues. The soft tissue intracellular compartments comprise about 38% of which higher concentrations are found in liver and skeletal muscle. (15-20 mEq/Kg). Less than 2% is present in extra cellular fluid (ECF) compartment.[23] Magnesium concentration in serum ranges from 1.7 to 2.4 mg/dL. (0.7 to1.0 mol/L). The plasma concentration in healthy adults remain remarkably constant.[7] It is pertinent to point out that limits of the normal range deviate by less than 15 percent from the mean, indicate that the serum concentration is maintained by sensitive control mechanisms, which are poorly understood at present.

Daily intake average magnesium is of the order of 25 mEq (140-360 mg/day). Dietary magnesium is absorbed less than 40% throughout the small intestine particularly in the ileum. Elimination is predominantly renal and averages 100mg/day. The upper limit of the normal range for urinary excretion is threshold. Thus, magnesium excretion increases dramatically when serum levels rise above 2.4 mg/dl, conversely, the kidney maintains a strong capacity to reabsorb magnesium when the condition of magnesium depletion prevails, The main site for re-absorption is the thick ascending renal re-absorption, such

as hypercalcemia, volume expansion and diuretic administration (eg. osmotic, thiazide or loop diuretics).24oop of Henle. Impairment of renal re-absorption may be caused by several factors.

BIOCHEMICAL IMPORTANCE OF MAGNESIUM

Magnesium is an important activator in a host of enzyme systems that are critical to cellular metabolism including hydrolyze and transfer phosphate groups, especially those involved in the reactions involving adenosine triphosphate (ATP). As ATP is necessary for glucose utilization, protein, fat, nucleic acid and co-enzyme synthesis, muscle contraction and other reactions by inference the activating effect of magnesium extends to all these functions. In addition to this, for oxidative phosphorylation in the mitochondria magnesium is required as a cofactor.[5]

Magnesium contributes significantly to macromolecular structure. The highly ordered organization of DNA, RNA and ribosome is stabilised by presence of this metal.[26,27] In protein synthesis also magnesium is involved by contributing to the binding of messenger RNA to the 70s ribosome.[28]

Interrelations of major biologic cations

- Magnesium generally found in high concentrations within the cell, where as the content calcium in the intracellular is low. The ratios are inverted

in extracellular fluid.[29]

- Variations in dietary calcium do not affect the absorption of magnesium.
- Magnesium reabsorption in renal tubules is inhibited by hypercalcemia.
- The intracellular phosphate concentration is usually parallel to magnesium concentration

Regulation of Serum Magnesium

Renal regulation

Regulation of concentration of serum magnesium is mainly achieved by control of renal magnesium reabsorption. About 20% of the filtered magnesium is reabsorbed in the proximal tubule, where as 60% is generated in the cTAL (thick ascending loop) and another 5-10% in DCT (Distal tubule). Magnesium reabsorption in cTAL is increased by parathyroid hormone and is inhibited by hypercalcemia and hypermagnesemia.7

Intestinal absorption

Around 30-40% of dietary magnesium (normally ranges from 140 – 360 mg/day) is absorbed, mainly in the ileum and jejunum. The efficiency of Intestinal magnesium absorption is stimulated by 1,25 (OH)2 Vitamin D and it can reach 70% during magnesium deprivation.[7,30]

Hormonal factors

Increasing serum magnesium,[30]

- Parathyroid hormone
- Glucagon
- 1, 25(OH) 2 Calcitriol.

Decreasing serum magnesium,

- Aldosterone
- Vasopressin (ADH)
- Thyroxine
- Calcitonin

Dietary Reference Intakes for Magnesium

Recommendations for magnesium are provided in the dietary reference intakes (DRI's) developed by the Food and Drug Administration (FDA).[31]Recommended Dietary Allowances (RDA) for magnesium are as per the table.

Table 6 :Recommended Dietary Allowances Magnesium values in mg/day).

AGE	MALE	FEMALE	PREGNANT	LOCATION
1-3	80	80	N.A	N.A
4-8	130	130	N.A	N.A
9-13	240	240	N.A	N.A
14-18	410	360	400	360
19-30	400	310	350	310
31+	420	320	360	320

Selected Food Sources of Magnesium content (in mg/100m)

Nuts like cashew contain 260,almonds contain315, peanuts175 mg/100mg

Split Beans contain 50 mg, soya bean-86mg/100mg of legumes

Fruits like banana contain 30mg/100mg, dates contains35mg/100mg,apple contains50mg/100mg of magnesium.

Milk product like butter contains20mg/100mg,Yogurt contains 12 mg/100mg, Milk contains24mg/100mg of magnesium. Cereals like wheat contains 10mg/100mg,Rice contains 40mg/100mg,meat and fish contains 20-22mg/100mg Greens like spinach contains highest concentration of serum magnesium. 22

Hypermagnesemia

Normal kidneys are capable of excreting large amount of magnesium upto 250mmol/day.Hence hyper magnesemia is a rare occurance.

Ca**uses of hypermagnesemia**

1. Due to decrease excretion of magnesium as occur in

- Chronic Renal failure and
- Familial hypocalciuric hypercalcemia

2.Increase intake of magnesium like

- Parenteral magnesium administration (eg.magnesium sulfate in

PIH)

- Laxatives
- Antacid preparations

3. Rapid magnesium mobilisation from soft tissues like

- sepsis
- Severe burns
- Extensive burns
- Shock,
- Post-cardiac arrest
- trauma

➢ Other disorders like

- Adrenal insufficiency
- Hypothyroidism
- Hypothermia

Clinical features

The most prominent clinical manifestation of hypermagnesemia depends upon serum level of magnesium 1. neuromuscular blockade and vasodilation, which appear at serum magnesium concentrations at > 4.8 mg/dL (>2mmol/L). Hypotension, refractory to vasopressors and expansion of volume, may be an early signs. Lethargy and weakness may progress to respiratory failure, paralysis and coma with hypoactive tendon reflexes (at serum magnesium is > 4

mol/L levels). Gastrointestinal hypomotility or ileus may occur. Prolongation of PR, QRS intervals, heart blocks and approaching the serum magnesium levels at 10 mmol/L, asystole.

Treatment

Generally involves identifying and avoiding the source of magnesium.Vigorous intravenous hydration and hemodialysis may be necessary. Calcium, given intravenously in doses of 100-200 mg over 1 to 2 hrs provides temporary improvement.

Hypomagnesemia

Hypomagnesemia signifies substantial decrease of body magnesium stores (0.5 to 1 mmol/Kg). Hypomagnesemia has varied etiology. Dietary magnesium deficiency is unlikely except in the setting of alcoholism.[24]

Causes of Hypomagensemia24

I. Impaired intestinal absorption

A. Primary infantile hypomagnesemia

B. Malabsorption syndromes

C. Vitamin D deficiency.

II. Increased intestinal losses

1. Protracted vomiting / diarrhea
2. Intestinal drainage, fistulae

III. Impaired renal tubular reabsorption

A. Genetic magnesium wasting syndromes.

1. Gitelman syndrome
2. Bartter syndrome
3. Na-K ATPase g-subunit mutations

B. Acquired renal disease

1. Tubulointerstitial disease
2. Post obstruction /ATN (diuretic phase)
3. Renal transplantation.

C. DRUGS

1. Ethanol
2. Diuretics (loop, thiazide and osmotic)
3. Cisplatin, cyclosporine
4. Aminoglycosides, Amphotericin B

IV. Metabolic causes

1. Hyperaldosteronism
2. SIADH
3. Diabetes mellitus
4. Metabolic acidosis
5. Hypercalcemia
6. Hyperthy roidism

V. OTHERS

1. Pancreatitis

2. Excessive sweating
3. Osteoblastic metastases

Several genetic magnesium wasting syndromes are explained, but are extremely rare. Protracted nasogastric suction, parenteral fluids, infected diarrhea, steatorrhoea, inflammatory and bowel disease may cause hypomagnesemia.33 Magnesium deficiency common in patients especially those who receives furosemide diuretic[34].

Frequency

Hypomagnesemia is a common entity occurs in up to 12% of hospitalized patients[35]. Incidence are known as high as 60% in patients in intensive care settings in which nutrition, hypoalbuminemia diuretics and aminoglycosides may play important roles.[36]

Risk of incidence is as follows:[37]

1. In general population2%.
2. In hospitalized patients10 – 20%.
3. In ICU patients. 50 – 60%
4. In Alcoholics30 – 80%.
5. In diabetic outpatients25%.

❖ Sex: Incidence is equal in males and females.

Clinical features[2,38]

History

- Presence of hypomagensemia can be found by obtaining history of potential causes (see table).
- Complaints related to hypomagensemia are nonspecific.
- Patients may have weakness, muscle cramping or rapid heartbeats.
- Altered mental status such as irritability, apathy, psychosis, delirium etc may be present in severe cases. Less severe cases may result in vertigo, ataxia, depression and seizure activity.

Physical signs

Symptoms and signs appear only when serum magnesium concentrations are <1.2 mg/dL (0.5 mmol/L). The primary clinical observations are neuromuscular irritability, cardiac arrhythmias and CNS hyperexcitability[39]

Signs

- Deep tendon hyperactive reflexes.
- Cramps of muscles.
- Trousseau and Chvostek
- Esophageal dysmotility causes Dysphagia
- Disorientation or Irritability
- Ataxia, seizures or nystagmus (at levels <0.8 mg/dl) Paroxysmal arterial and
- ventricular dysrhythmias.

ECG

Depletion of magnesium can induce changes in the electrocardiogram. Findings in hypomagnesemia are nonspecific. Modest magnesium depletion (1.2 to 1.7 mg/dl) leads to widening of QRS complex with peaking T-waves, while more severe magnesium deplection (<1.2 mg/dl) is associated with protracted PR interval, progressive widening of QRS complex, flattening / inversion of T-waves and U waves.40 Cardiac arrhythmias may occur including sinus tachycardia, other ventricular arrhythmias and supraventricular tachycardia.

Lab Studies

The serum magnesium level cannot a reliable determinant of total

magnesium depletion in the body because only a small fraction of magnesium in the body is extra cellular. However, if serum level is low indicates a clear deficiency of magnesium. [41]

Serum magnesium levels may be estimated by several methods.

- Neutron activation analysis
- Atomic absorption spectrometry
- Ion selective electrodes (ISE)
- Equilibrium dialysis
- Calmagite dye method.

Calcium, potassium and phosphorous levels must be assessed.

- BUN and creatinine levels.
- Blood glucose level.

Treatment

The mechanism of magnesium repletion varies with severity of the clinical manifestations. As an example, the hypocalemic-hypomagnesemic patient with tetany or the patient with hypomagnesemic ventricular arrhythmias should receive 50 mEq of IV magnesium slowly over a period from 8 to 24 hours. To maintain plasma magnesium concentration above 1.0 mg/dl.42, this dose can be repeated as necessary

In less critical patients, oral replacement should be given preferably with

a sustained release preparation. There are several such preparations available such as Slow Mag (magnesium chloride) and MagTab-SR (Magensium lactate). These preparations can give 60-84mg (2.5 to 3.5 mmol) per tablet. For severe magnesium depletion (<1.2mg/dL) six to eight tablets should be taken daily in divided doses. For milder disease two to four tablets are enough to control. If necessary, addition of potassium sparing diuretic in those who cannot discontinue diuretic therapy, discontinuation of diuretic therapy,, treatment of chronic diarrhea etc.[2]

HYPOMAGNESEMIA AND DISEASE CORRELATES

Magnesium and cardiovascular diseases

The close associations of magnesium metabolism, diabetes and high blood pressure may likely to cardiovascular disease.

Arrhythmia

Magnesium depletion can also induce change in the electrocardiogram. But, there are conflicting data as to whether hypomagnesaemia is associated with arrhythmia in otherwise healthy subjects. It is learnt that a study over 3000 patients from the Framingham Heart suggests that the manner in which arrhythmia is defined is an important determinant.[40] No association with hypomagnesemia was noted for more than 10 ventricular premature complexes (VPC) per hour or for repetitive VPC. Nevertheless, an increased risk of

complex or frequent (>30/hr) VPC with reduction in plasma magnesium concentration of 0.2 mg/dL (0.08 mmol/L) or more. The clinical disturbance of greatest potential importance is however, the association of mild hypomagnesemia with ventricular arrhythmias in patients with cardiac disease. A number of uncontrolled studies suggest that hypomagnesaemia may be an important risk factor for arrhythmias in the setting of an acute ischemic event, torsade de pointes and congestive heart failure, after cardiopulmonary bypass or in acutely ill patient in the intensive care unit.[43,44]

Arrhythmias could be due to hypomagnesemia itself, concurrent hypokalemia, or both. Magnesium regulates and maintain several cardiac ion channels, including the calcium channel and outward potassium currents.45 Lowering of cytosolic magnesium concentration will markedly increase these outward currents, shortening the action potential and increasing susceptibility to arrhythmias.

Torsade de Pointes

Magnesium sulfate can be added for the management of torsade de pointes, or refractory ventricular fibrillation.[46] as recommended by the American Heart Association, 1992 and gives guidelines for Cardio pulmonary resuscitation and emergency cardiac care. Torsade De pointes is a unique ventricular tachycardia most commonly precipitated by drugs that prolong the QT interval (e.g. Quinidine), electrolyte imbalance (hypokalemia and

hypomagnesemia), or a slow heart rate. Treatment has to be done with an aim of accelerating the heart rate and/or shortening the QT interval. Treatment of intravenous magnesium is now considered even when hypomagnesemia is not present.[42]

Hypertension

Magnesium has playing important role in reducing blood pressure.[47] It is a antagonist of calcium and important activator of sodium potassium ATPase When the serum magnesium level decreases which in turn lead to raising intracellular concentrations of calcium and potassium, which in turn causes increase in peripheral vascular resistance and vasoconstriction.

Magnesium may also have a direct impact on vascular smooth muscle.[48] In one study of clinical trial 73 patient selected by random methods, subjects not taking oral diuretics or other pharmacological drugs affecting the metabolism of magnesium, Petersen et al found the relation between serum magnesium level and blood pressure was an inverse correlation.49

Additingly, research showed that patients with hypertension having hypomagnesemia frequently needs more antihypertensive drugs than hypertensive patients with normal magnesium levels. In another study using placebo controlled trial, showed magnesium supplementation in patients taking

long term oral diuretic treatment for systemic hypertension, achieved noticeable decrease in blood pressure, by average of 12mmhg in systolic and diastolic pressure of 5mmhg.

The Joint National Committee (JNC) for recommendation for prevention, detection, evaluation treatment of high blood pressure stress the importance of maintaining an adequate level of magnesium intake as a positive changes in life style modification for preventing and managing high blood pressure.

Magnesium and ischemic heart disease

Some observational surveys showed in their studies, higher blood levels of magnesium associated with lower risk in the incidence of coronary artery disease. Two studies, prospective epidemiological studies involving large people, have examined the relationship between the serum magnesium level and development of coronary heart disease subsequently. They suggested that a low level of serum magnesium is a important risk factor for the development of coronary artery disease.[52,53] One study, involving15,792 people, in observational study, examined and followed the subjects in the age group of 45 to 64 years, for a seven year period as part of the Atherosclerosis Risk In Communities Study (ARIC). They found that both men and women who developed CHD had serum magnesium concentration at a lower mean level than the disease free controls. The relative risk of CHD across the quartiles of serum magnesium concentration decreased from lowest quartile to higher quartiles. But

pathophysiologic mechanism causing low serum magnesium that might predispose to coronary heart disease is not known.

Many smaller studies also suggested that supplementation of magnesium may lead to improvement in the exercise tolerance, may have an additional protective antithrombotic effect with drug like aspirin and may causing improvement in clinical outcomes in individuals suffering from coronary artery disease

Acute Myocardial Infarction

Acute MI is frequently associated with marked reduction in serum magnesium concentraion.[55] Mild decrease in serum magnesium associated with acute myocardial infarction appears to give rise to a 2 to 3 fold increase in the incidence of ventricular arrhythmias in the first twenty four hours period, in related to those with presence of normal serum magnesium levels.[44] A study done by Uncontrolled trial method suggested that the administration of parental magnesium at this time can decrease the frequency of potentially fatal outcome of ventricular arrhythmias.

A relationship has also been found between ventricular arrhythmias and levels the plasma magnesium and occurring in the second or third week after myocardial infarction. In one study stats that in patients with no abnormal rhythm, the average level of plasma magnesium concentration was 1.83 mg/dl,and in patien with multifocal ventricular premature complexes the level

of serum magnesium was1.68 mg and 1.55 mg/dl in patient suffering from un sustained ventricular tachycardia. Complex arrhythmias are seen in thirteen patient and hypomagnesemia was found out corrected with intravenous magnesium; and normal sinus rhythm was restored.

Magnesium and congestive heart failure:

In patients suffering from congestive heart failure an increased incidence of hypomagnesaemia has been found repeatedly. and is mainly due in part to therapy diuretic drugs. A role for magnesium depletion in sudden death has been suggested but pathophysiological mechanism that causes death is not proven. No correlation was found between hypomagnesemia and class III or IV heart failure in a prospective study attended by more than 1000 patients done at the beginning of the study and survival at a median follow up of 6 months.

- Osteoporosis- In postmenopausal women magnesium deficiency may play an additional risk factor for development of osteoporosis. It may be noted that magnesium deficiency is altered with calcium metabolism and the hormones that regulate the calcium metabolism. Several human studies have suggested that bone mineral density may improve with. magnesium supplementation.
- Dietary surveys have proved that a increased level of magnesium intake is associated with decreased incidence of cerebrovascular disease

- **Asthma:** Magnesium plays a important role in maintenance of lung structure and function. Magnesium acts by blocking the function of calcium, which leads to contraction of bronchial smooth muscle .[62]The decreased magnesium level also has an effect on immune response. A diet high in magnesium is directly related to healthy lung function and a reduced risk of airway hyper reactivity. Increase in the incidence of bronchia; asthma associated with hypomagnesemia.[63]
- **Parathyroid hormone resistance**: Studies have shown that the decrease in serum magnesium level interferes with improvement in hypocalcemia in response to parathyroid hormone and symptomatic hypocalcemia is almost always associated with serum magnesium levels below 1.2 mg/dl (0.5 m mol/L).64
- Magnesium depletion is also related to increased plasma LDL, cholesterol and tirglyceride and reduced plasma HDL.[65]

Magnesium and diabetes

Magnesium ion has a fundamental role in the metabolism of carbohydrate metabolism and Diabetes mellitus has been suggested to be the most common metabolic disorder associated with magnesium deficiency, with the of 25 to 39% [5,6,7]

The clinical implications of magnesium deficiency as it relates to diabetes

are many. Hypomagnesemia as a consequence un-contolled of hyperglycemia (associated with increased urinary magnesium excretion along with glycosuria) and a cause resistance of insulin. The relation between diabetes mellitus and hypomagnesaemia is compelling for its wide ranging impact on hyperglycemic control, complications, and ultimately therapy. Although poor glycemic control is associated with magnesium deficiency, it is not simply induced by hyperglycemia and is not corrected by improvement in metabolic control alone. Magnesium depletion has been associated with the development of diabetic retinopathy.[10] Of greater importance is the association between decrease in magnesium level and systemichypertension,[5066 66] insulin resitance thrombotic tendency,[66,67] and the Reaven – Modan syndrome, a rare clinical entity that links diabetes mellitus, hyperinsulinemia, [68]increased thrombotic tendency hypertension and tendency – all cardiovascular risks.

Causes of hypomagnesemia in diabetes mellitus

Initially, the cause of hypomagnesemia in diabetes was attributed to (1) o glycosuria due to osmotic renal losses (2) decreased in intestinal magnesium absorption and (3) due to insulin effect there is redistribution of magnesium from plasma to red blood cells. Recently a specific tubular magnesium defect in diabetes has been postulated. A reduction in tubular absorption of magnesium results in hypermagnesuria. The exact site of re-absorptive defect is not yet defined. This is postulated to be either in the thick ascending loop of Henle or

more distal loop of Henle.

The cause of this tubular defect in magnesium resorption also is not clear. Insulin treatment has been shown to correct diabetic renal losses of magnesium .The delayed insulin treatment may be less effective in correcting the renal electrolyte losses, suggesting some irreversible component.

The role of magnesium in insulin action

Magnesium is involved in various levels in insulin secretion, binding and activity. Magnesium is a important cofactor of many enzymes involved in carbohydrate metabolism.

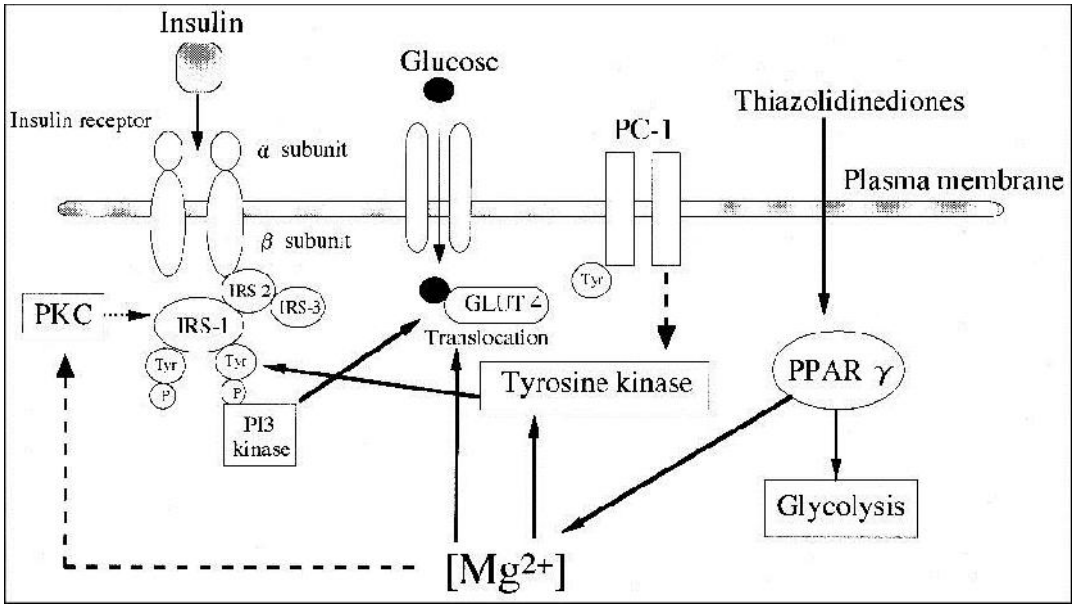


Figure 24 : Mechanism of action of Mg

In addition to these effects of magnesium, magnesium deficiency has

been shown to associated with insulin resistance in multiple studies.

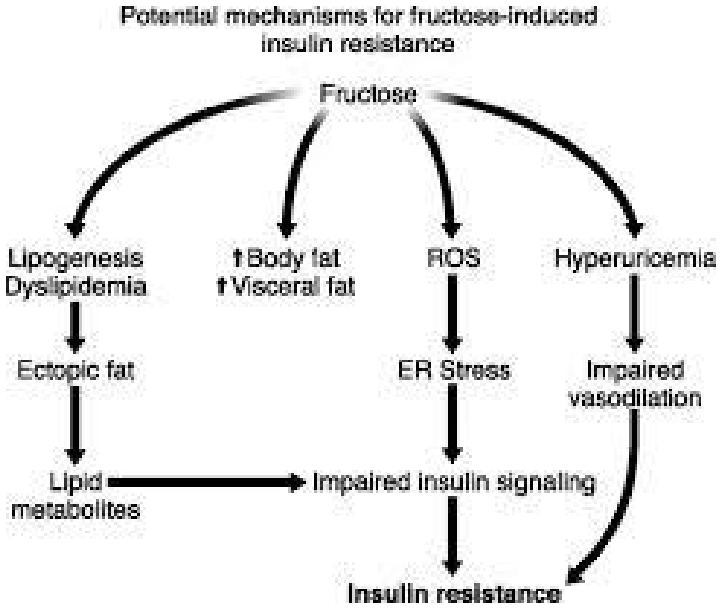


Figure 25: Relationship between Glucose and Insulin resistance

In a recent study, Attenuation of the cellular uptake of magnesium, which is normally stimulated by insulin, was present in patient with diabetes..

There is also evidence that magnesium deficiency itself produces insulin resistance. Nadler et al.[8] studied 16 non diabetic subjects and found that insulin sensitivity felt after induction of magnesium deficiency.

Likewise, in elderly non-diabetic normo-glycemic subjects were shown to have improved glucose handling, when they take regular magnesium supplements for 4 weeks.74 There was a direct relationship between intracellular magnesium concentration and glucose metabolism, thus implicating magnesium deficiency in the insulin resistance of aging. In non

diabetic obese subjects, insulin resistance was found along with low magnesium levels, when compared with non obese subjects, again highlighting the association between hypomagnesemia and insulin resistance.[75]

An intriguing theory, suggested by Tonyai, et al.[76] is that membrane viscosity may altered with a low erythrocyte magnesium content , and this may reduce the interaction of insulin with its receptor on the membrane. Paolisso et With the long-term of magnesium administration can reduce membrane micro viscosity

.

Role of magnesium deficiency in diabetic end organ damage

Magnesium deficiency has been frequently found to be associated with diabetic microvascular disease. Decrease level of has been demonstrated in patients with diabetic retinopathy, with lower serum magnesium levels associated with a greater risk of severe diabetic retinopathy.[10] Magnesium depletion is also found to play a role in patient with diabetic polyneuropathy. Corsonello, et all have reported an association between diabetic nephropathy and magnesium depletion.

Microalbuminuria and clinical proteinuria, as well as poor glycometabolic control and hypertriglyceridemia, are associated to relevant alterations in serum ionized magnesium.

Magnesium depletion has been associated with multiple cardiovascular

complications: arrhythmias, vasospasm, hypertension and platelet activity.[43,50]

Three exciting theories link diabetes and its vascular complications to hypomagnesemia: the inositol transport theory, oxidative stress and the ionic hypothesis of metabolic disease

Grafton, et al[14] have focused on the inositol transport theory. It has been one of the favored explanations for the origin of diabetic complications.

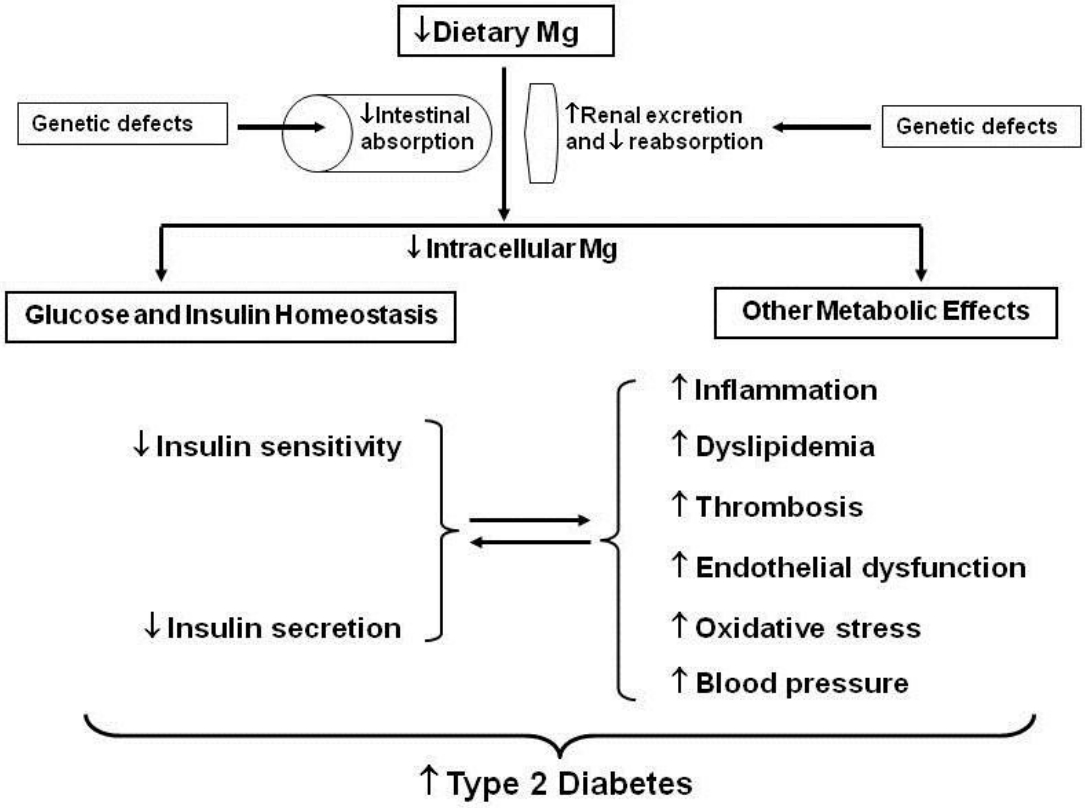


Figure 26: Role of Mg in Type 2 DM

The association between magnesium deficiency, essential hypertension, insulin resistance, hyperinsulinemia[68], and ischemic heart disease (Reaven-Modan Syndrome) may be proved by the ionic hypothesis of cardiovascular and metabolic disease, proposed by Resnick.

:

Table 7: Causes of Mg deficiency

Decreased absorption:	Intestinal resection, cardiac disease, chronic diarrhea
Non renal loss:	Chronic vomiting, Nasogastric aspiration, Excessive lactation, villous adenoma.
Renal loss:	Salt losing nephropathy, Barters syndrome, renal tubular acidosis, alcoholism, diuretic therapy, Glycosuria.
Endocrine:	Diabetes mellitus, Hyperparathyroidism, Post- parathyroidectomy.

Diabetes is a state of increased free radical activity.

Figure 27: showing Mg rich food

Magnesium deficiency has been shown to reduce functions of natural antioxidants like glutathione, ascorbic acid and Vitamin E.

EVIDENCE FOR EFFICACY OF MAGNESIUM SUPPLEMENTATION IN DIABETES MELLITUS

There is more number of evidence that repletion of magnesium can ameliorate the insulin resistance, platelet reactivity and other cardiovascular risk factors associated with hypomagnesemia and diabetes mellitus.[78]

In a study of 16 diabetics and 30 healthy controls, oral replacement with magnesium hydroxide at a dose of 250mg twice daily resulted in decreased insulin requirements in the diabetic patients. In elderly type 2

diabetics,Paolisso,[74] et al demonstrated that oral magnesium supplementation given for four weeks resulted in lower the fasting plasma glucose levels, increased plasma magnesium levels and though a slight, but statistically significant increase in beta-cell response to glucose and arginine. In type 2 diabetics, oral supplementation of magnesium has been shown to decrease platelet reactivity, lower systolic blood pressure by 7 mm Hg and to result in a beneficial effect on lipid profile.

CLINICAL APPROACH TO MAGENSIUM SUPPLEMENTATION IN DIABETES MELLITUS

The consensual conference on magnesium supplementation sponsored by the American Diabetes Association warrants a more interventionist approach to hypomagnesemia.

There are no accurate tests clinically available to determine intracellular magnesium depletion routinely in diabetics. With 99% of the body stores of magnesium being intracellular, low serum magnesium level is an insensitive, yet precise measure of total body stores. Certainly, patients at risk for hypomagnesaemia should have serum magnesium measured. This includes diabetics with clinical states known to be associated with hypomagnesaemia such as, ketoacidosis, alcohol abuse, long term parenteral nutrition, chronic diarrhea or use of diuretics, acute myocardial infarction, ketoacidosis / digoxin.

Additionally, patients at high risk of cardiac events such as arrhythmia and vasospasm, should be considered for magnesium replacement.

Whether the broader range of magnesium related abnormalities, such as hypertension, hyperlipidemia and insulin resistance of diabetes itself, should be treated with repletion requires a randomized clinical trial to determine. However, each patients individual risks for hypomagnesemia, cardiovascular risks and risks related to therapy need to be assessed. Overt serum hypomagnesaemia should always be corrected. If hypomagnesemia is clinically suspected, but cannot be documented by serum levels, a further test with erythrocyte or platelet magnesium concentration is necessary. Renal insufficiency, especially with creatinine clearance of less than 30 ml/min is the only factor that precludes dietary supplements. Magnesium chloride is the preparation of choice (Slow Mg). Doses of 100 to 600mg/day may be necessary to correct repletion. Diarrhea is the dose limiting side effect

METHODOLOGY

Source of data

Patients with type 2 diabetes attending in Chengalpattu Medical college& Hospital, Chengalpattu, Kanchipuram district, , over a period of one year between 1st September 2013 to 30th to September 2104.

Sample size

The sample size was 100 patients.

Study population

One hundred randomly selected patients with type – 2 diabetes mellitus on oral hypoglycemic agents (OHAS) and/or insulin treatment attending as in or out patients in Chengalpattu medical college& Hospital constituted the study population.

Out of these, 67 were men and 33 were women. The mean age of subjects was 58.3 years with a range of (40-78) years. The median (range) duration of diabetes was 5.5years (01-22 years). Of these patients, 69 patients were receiving OHAs alone, 5 patients insulin alone and 20 were receiving both insulin and OHAs. 32 of these subjects had hypertension and 16 had coronary heart disease. Patients with renal failure, acute myocardial infarction, patients

on diuretics, alcoholics or with mal-absorption were excluded. None were taking magnesium supplements or magnesium containing antacids. Consent was obtained.

Inclusion criteria

All patients suffering from type 2 diabetes mellitus admitted in in Chengalpattu medical college& Hospital .

Exclusion criteria

1. H/O. Patients suffering from chronic renal failure.
2. H/O Acute myocardial infarction for last 6 months.
3. Patients is on diuretic drug therapy
4. Patients with h/o of alcohol abuse.
5. Patients receiving magnesium supplements or magnesium containing antacids.
6. Mal-absorption or chronic diarrhea

Data collection

The 100 diabetics (with median diabetic history of 5.5 years) were included in the study. Detailed history – including duration of diabetic illness, mode of treatment ,symptoms suggestive of diabetic retinopathy nephropathy , associated diseases such as systemic hypertension and ischemic heart disease were obtained, as per the proforma.

Followed by physical and neurological examination, and ECG. Retinopathy was assessed by direct opthalmoscopy. Blood specimen were collected for testing of fasting blood glucose and plasma magnesium. sugar was measured two hours after a standard meal. Blood urea, serum creatinine and 24 hour urinary albumin were estimated. Serum magnesium was estimated by Calmagite dye method. HbA1C was measured.

Calmagite dye method for quantitative estimation of serum magnesium

Test principle

Under alkaline conditions, magnesium ions react with calmagite dye to produce a red complex which is measured spectrophotometrically at 530 nm.

Intensity of the colour produced is directly proportional to magnesium concentration in the serum. To eliminate the interference of calcium during estimation, EGTA is included in the reagent.

Test procedure

These test tubes are incubated at room temperature (22-28ºC). The absorbance of Test (AT), Standard (AS) and Blank (AB) are read at 530nm spectrophotometer. Magnesium concentration is calculated by the following formula.

In test	Blank	Standard	Test
Calmagite	1.0ml	1.0ml	1.0ml
Patient sample		10ml	10ml
Standard			
Distilled water	10.0ml		

Magnesium concentration (mEq/L) = (AT-AB / AS-AB) x 2

Serum magnesium concentration is expressed in mg/dl by

linearity of 1 mEq/L = 1.2 mg/dl.

Subsequently patients were divided into three groups based on their following values: Normal, 1.7 to 2.4 mg/dl, low <1.7mg/dl, high >2.4 mg/dl. Patients were also categorized on the basis of duration of diabetes, presence of ischemic heart disease or systemic hypertension, mode of treatment, presence/absence of retinopathy, neuropathy and nephropathy, and glycemic control (FBS and HbA1C). Patients with diabetic retinopathy were further classified as those with non-proliferative diabetic retinopathy (NDPR) and those with proliferative diabetic retinopathy (PDR). Diabetic nephropathy was graded depending on 24 hour urinary excretion of albumin as follows: No nephropathy,

< 30mg/24hour, microalbuminuria 30 – 299mg/24hour and macroalbuminuria (clinical proteinuria) >= 300 mg/24hour.

Statistical method

Statistical method analysis was done using Chi-square test and Fisher's exact test to compare proportions. Statistical results were considered significant at P value < 0.05

RESULT

100 persons affected by type – 2 diabetes (68 male, 32 female, mean age 58.5 years) comprised the study group. These patients were further grouped with regards to their age, course of the disease, mode of diabetic management, glycemic control, presence / absence of comorbidities (present of heart disease and hypertension) and presence / absence of diabetic complications (diabetic retinopathy, diabetic neuropathy and diabetic nephropathy).

Table No. 9: Age Distribution

Patients were distributed across the age spectrum of 40 to 78 years. Mean age of the patients was 58.30 years. Most patients (n=36) were in the age group of 51-60 years. Youngest patient was 38 years old.

Table: 8 Age Distribution

SI.No	AGE GROUP	No. of Patients
1	<40	1
2	41-50	16
3	51-60	36
4	61-70	33
5	>71	14

Graph 1: Age Distribution

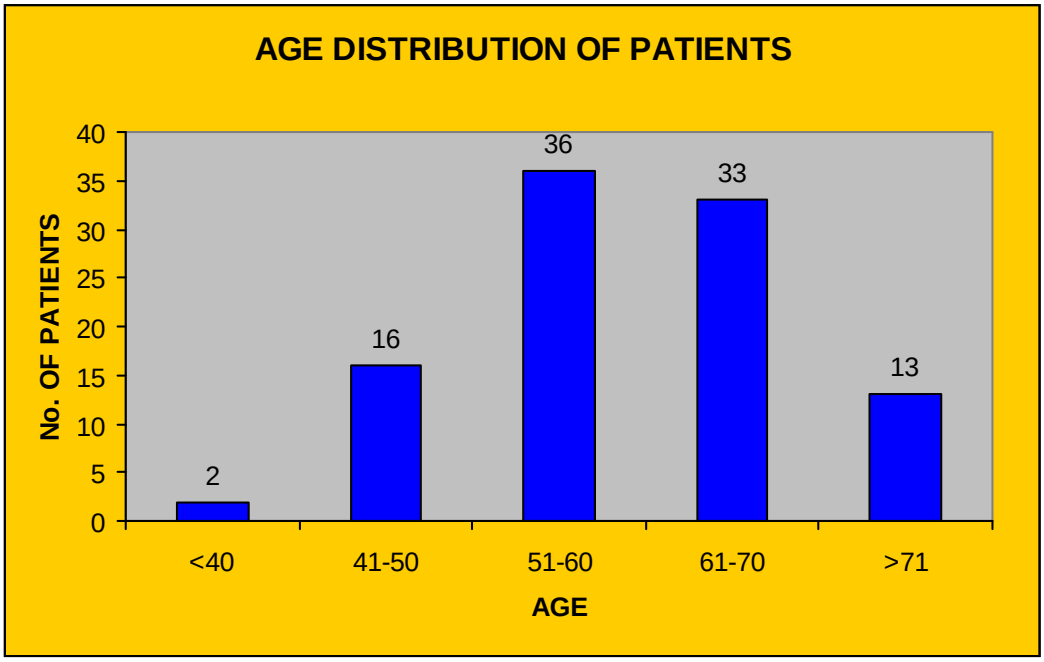


Table 9: Characteristics of study population

SI.No	Characteristics of population	values
1.	No of people examined	100
2.	Age in years	58.3(40-78)
3.	Men	67
4.	Women	33
5.	Duration of diabetes	5.5(01-22)
	MEDICATION	
6.	Insulin	05
7.	Oral Hypoglycemics	69
8.	Insulin and oral hypoglycemic	26
9.	Diet only	00
	Co morbidities	
10.	Hypertension	32
	Diabetic retinopathy	37

11.	Non proliferative diabetic retinopathy	33
	Proferative retinopathy	04
	Diabetic nepharopathy	18
	Microaibumineria	15
	Macroalbumineria	03

CHARACTERISTICS

The average duration of diabetes in study population was 5.5 years and range was 1 year to 22 years. As for the mode of diabetic treatment, 5 patients received only insulin, 69 patients only oral hypoglycemic agents and 26 patients received both. 32 patients had hypertension and 16 patients had ischemic heart disease and 56 patients had no comorbidities. Total 37 patients had diabetic retinopathy and out of them, 33 had nonproliferative diabetic retinopathy and 4 had proliferative diabetic retinopathy.. 18 patients had diabetic nephropathy; 15 had microalbuminuria (30 – 299 mg/d) and 3 had clinical proteinuria (> 300 mg/d). 68 patients were found to have poor glycemic control defined as HbA1C > 7%

Table10: Prevalence of hypomagnesmia in study population

Sl.No	Sex	No. of Patients	Hypomagnesimia	Percentage
1	Male	67	19	28.4
2	Female	33	12	36.4
Total		100	31	31

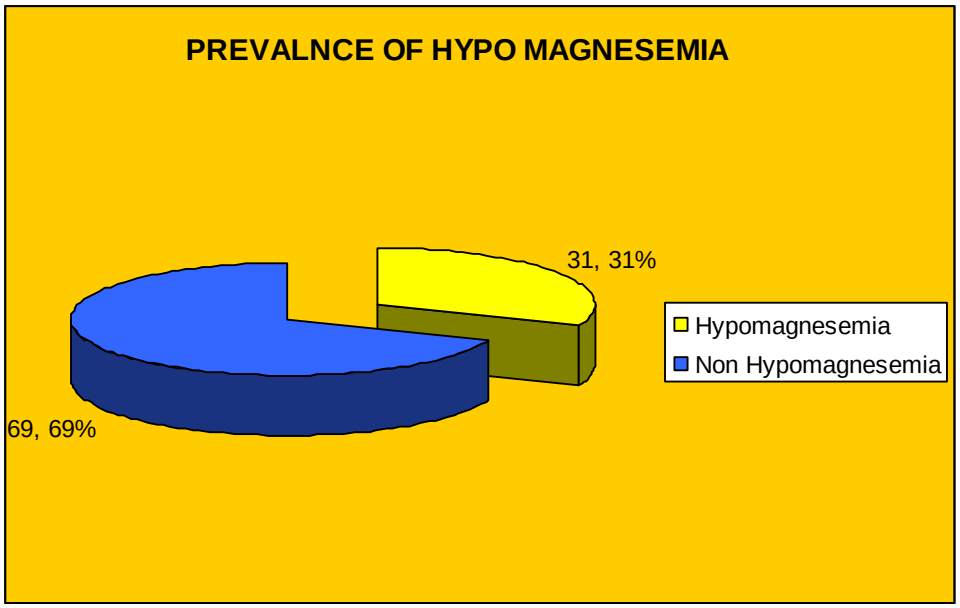


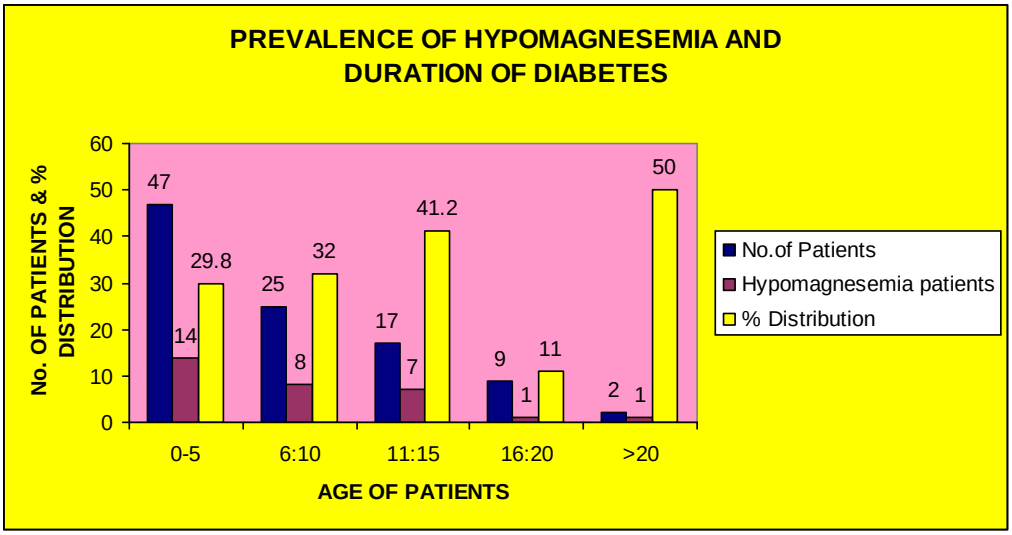
Table:11 Prevalence of Hypomagnesemia and Duration of diabetes

Sl.No	Duration of Diabetes	No.of Patients	Hypomagnesemia patients	% Distribution
1	0-5	47	14	29.8
2	6:10	25	8	32
3	11:15	17	7	41.2
4	16:20	9	1	11
5	>20	2	1	50

Hypomagnesemia (defined as fasting serum magnesium concentration < 1.7 mg/dl) was found in 31 patients. 69 patients had normomagnesemia. No patient had hypermagnesemia.

No significant difference was found in the rate of hypomagnesemia in men and women (28.40% and 36.40% respectively). Mean serum magnesium concentrations were also similar in men and women.

Graph: 3

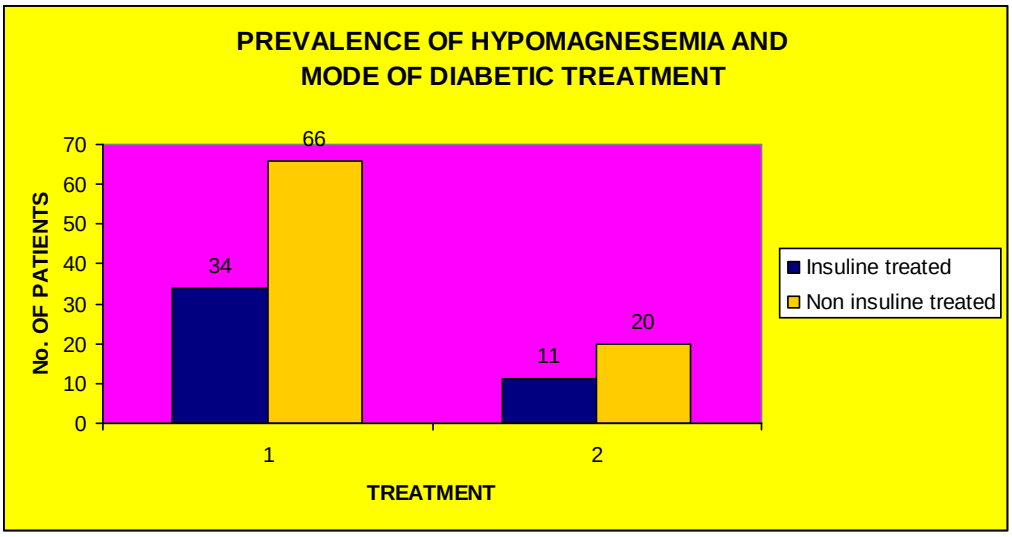


The average course of the disease was 5.5 years (01-22 years). The chi-square ($\chi 2$) value is 0.769 and P value is 0.586 at 4 degrees of freedom. So the correlation is insignificant at P value 0.05. So, the duration of diabetes did not significantly predict serum magnesium concentration

Table 12: Prevalence of hypomagnesemia and mode of diabetic treatment

Treatment	No of patients	Hypomagnesemia	% distribution
Insuline treated	34	11	32.35
Non insuline treated	66	20	30.3

Graph: 4



Hypomagnesemia

A higher prevalence of hypomagnesemia was observed in patients treated with insulin. However, the difference was statistically insignificant. $\chi 2$ value of 0.033 and P value of 0.855 at degree of freedom 1.

PREVALENCE OF HYPOMAGNESEMIA AND FASTING BLOOD SUGAR

Table 13:

FBS	No. of Patients	Hypomagnesemia	% Distribution
<90	6	1	14.29
91-100	15	3	20
101-110	21	2	9.51
111-120	20	8	40
121-130	16	7	43.75
>130	22	10	45.45

Graph 5

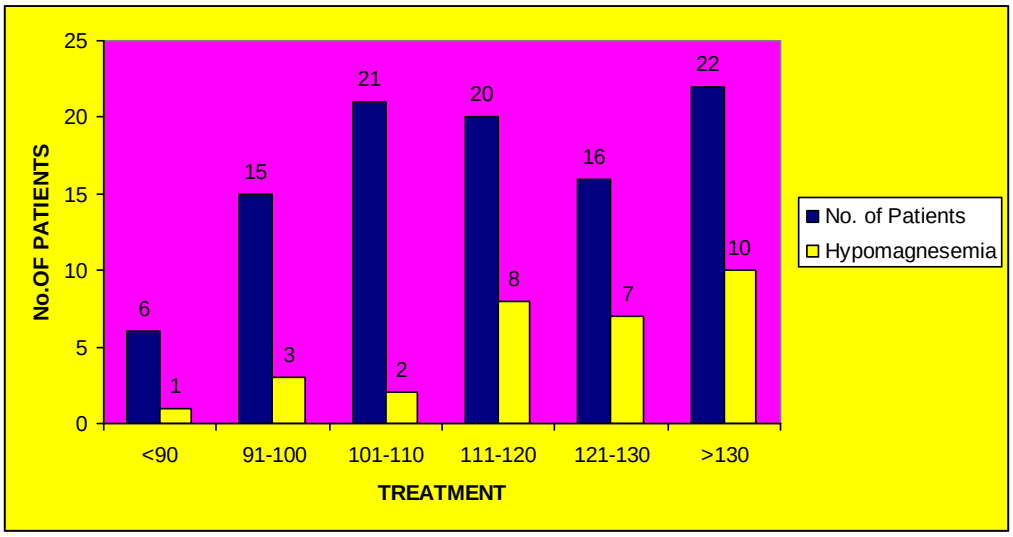
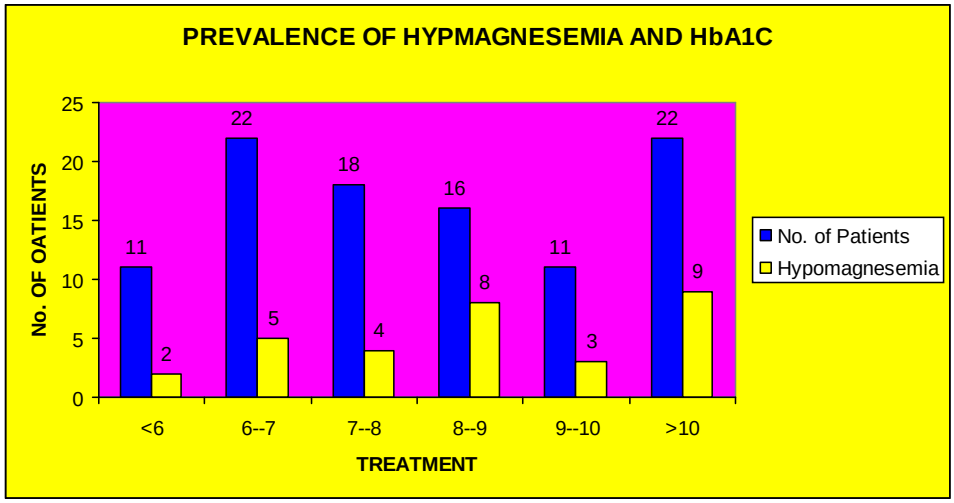


Table 14: PREVALENCE OF HYPOMAGNESEMIA AND HbA1C

HbA1c	No. of Patients	Hypomagnesemia	% Distribution
<6	11	2	18.18
6--7	22	5	22.73
7--8	18	4	22.22
8--9	16	8	50
9--10	11	3	27.27
>10	22	9	40.91

Graph:6



Hypomagnesemia

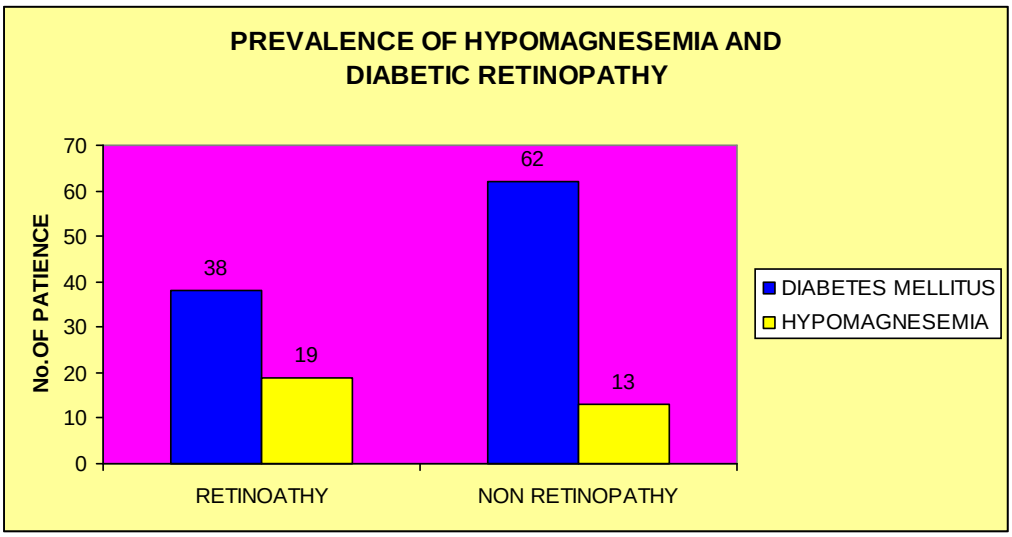
Serum magnesium concentration showed no significant correlation with fasting blood sugars or with HbA1C, though a higher prevalence of hypomagnesemia was found with higher fasting sugar (> 130 mg%) and Hb1AC

(> 7%). For FBS, χ^2 = 10.412, P = 0.064, DF= 5 and for Hb1AC, χ^2 = 9.728, P = 0.083 and DF=5.

PREVALENCE OF HYPOMAGNESEMIA AND DIABETIC RETINOPATHY

Table 15

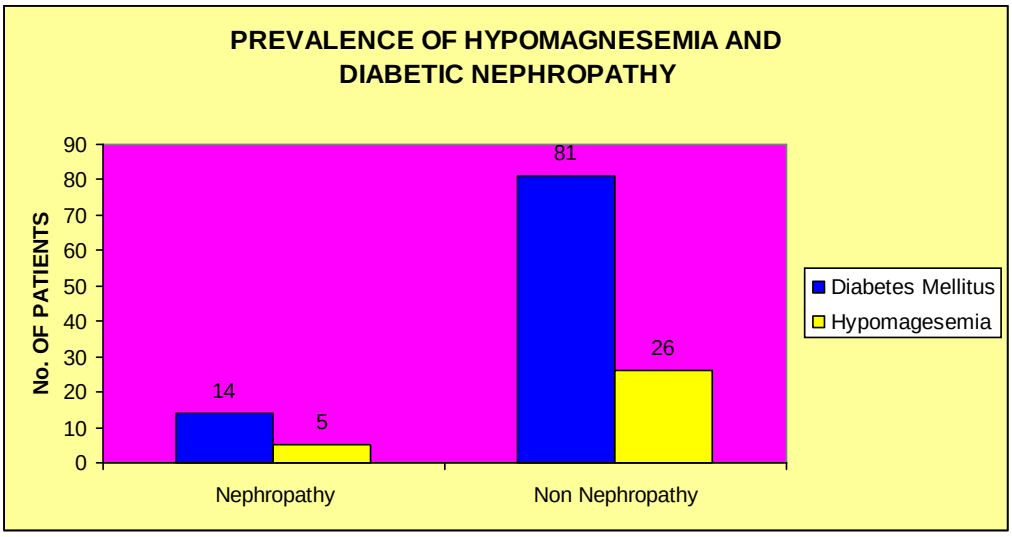
Retinopathy	No. of Patients	Hypomagnesemia	Normo Normomagnesemia
NPDR	33	16	17
PDR	5	3	2
Total	38	19	19
Non Retinopathy	62	13	12



Observations revealed a definite correlation between hypomagnesemia and diabetic retinopathy. Patients with diabetic retinopathy had a significantly higher prevalence of hypomagnesemia compared to patients without retinopathy (51.30% v/s 19.00%) and more over patients who had retinopathy were found to have lower mean serum magnesium level than those without retinopathy(17.4mg/dl v/s 18.2 mg/dl). The difference was statistically significant ($\chi 2$ value 9.911 and P value 0.002 (< 0.05) at degree of freedom 1).

Table16: PREVALENCE OF HYPOMAGNESEMIA AND DIABETIC NEPHAROPATHY

Nephropathy		No.of Patients	Hypo magnesemia	Normo magnesemia
Nephropathy	Microalbuminuria	14	4	28.57
	Macroalbuminuria	5	1	20
	Total	19	5	26.32
Non Nephropathy		81	26	32.1



The difference in prevalence rates of hypomagnesemia in patients with nephropathy and without nephropathy had no statistical significance ($\chi 2$=0.106, P = 0.744, DF=1).

TABLE: 17 PREVALENCE OF HYPOMAGNESEMIA AND HYPERTENSION

HTN	No. of Patients	Hypomagnesemia	% of Distribution
HTN	34	8	23.53
No HTN	66	23	34.85

Graph:9

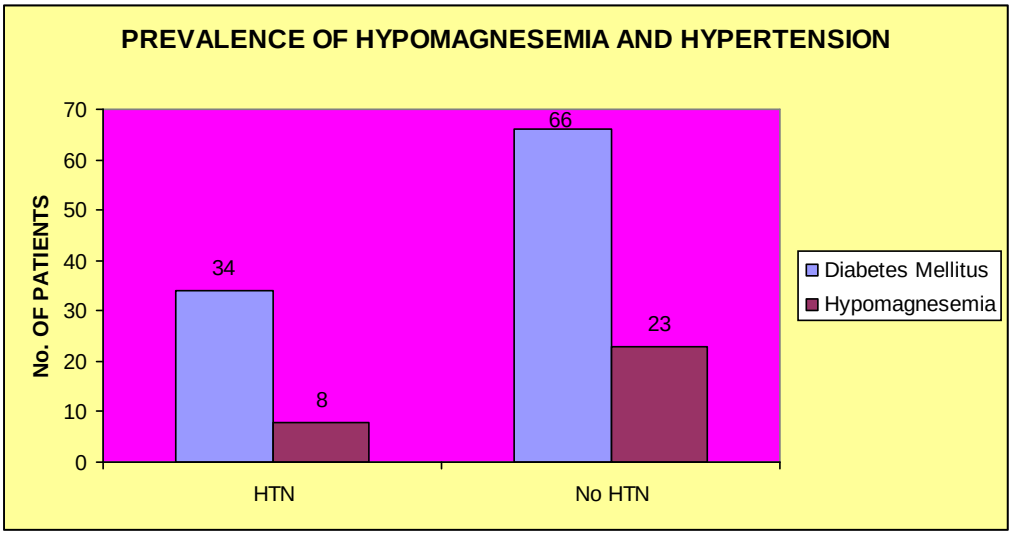
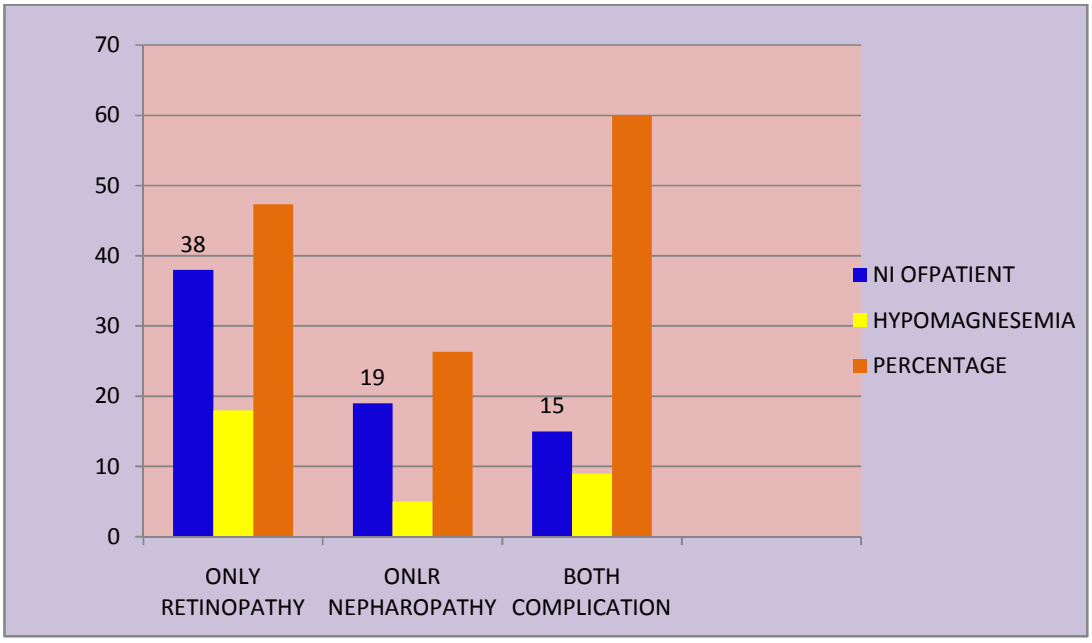


Table: 18. PREVALENCE OF HYPOMAGNESEMIA AND DIABETIC COMPLICATIONS

Complication	No of patient	**Hypomagnesemia**	**Percentage**
Only Retinopathy	**38**	**18**	**47.36**
Only nepharopathy	**19**	**5**	**26.31**
Both complication	**15**	**9**	**60**



Prevalence of hypomagnesemia in diabetics with complications was significantly higher compared to diabetics with no complications (45.24% versus 20.68%). The difference was statistically significant ($\chi 2$ value is 6.863 and P value 0.008 at DF of 1). In addition, average serum magnesium concentration in patients with diabetic complications was relatively lower than in diabetics without any complication (1.72 mg/dl and 1.84 mg/dl). Among the diabetics with complications the prevalence of hypomagnesaemia was not significantly different in groups of patients with only retinopathy, only neptharopathy, retinopathy with nephropathy or all three complications ($\chi 2$ value is 0.8922 and P value 0.684 at DF of 3). Among the patients with hypomagnesemia, prevalence rate of hypertension, diabetic nephropathy and poor glycemic indices were comparable to normomagnesemic group. However, conclusively higher prevalence of diabetic retinopathy was found in hypomagnesemic patients compared to normomagnesemics (61.30% versus 26.00%).

DISCU**SSION**

Widespread presence of low level of serum magnesium noted, among these patients and presence of association between hypomagnesemia and diabetic complications elicitable from this study.

Severe magnesium deficiency has been noticed in the previous studies in patients with type-2 diabetes. , some workers have also reported high and even low levels. In the present study, serum magnesium concentrations of 31 patients with type 2 diabetes, were below the reference range. This confirms to the reported the presence of low plasma magnesium status in type-2 diabetics in many studies, which are ranged from 26 to 38%. Prevalence of hypomagnesemia in type – 2 diabetics in our study was similar to that reported by Nadler et al.5 in type 2 diabetics attending outpatient clinics in the US. Walti MK et al. also reported a prevalence of hypomagnesemia in type 2 diabetics conduced at Zurich, Switzerland 37.6% versus 10.9% in nondiabetic controls.

Magnesium is present mainly as an intracellular cation, with less than one persent of total body content present in the extracellular fluids. The magnesium concentration in serum represents less than 0.3% of total body magnesium. however, though less sensitive presence of low level of serum magnesium concentration , is a highly specific indicator of. In addition, serum

magnesium measurement is the most readily available and widely used test of magnesium status.

The reasons for the increase prevalence of magnesium deficiency in diabetes though not clear, but may include increased urinary excretion, low level of dietary intake, or decreased absorption of magnesium when compared to healthy people. Several studies have noticed increased urinary magnesium excretion in both type 1 and type 2 diabetes. Recently a specific tubular defect has been noticed in magnesium reabsorption in thick ascending loop of Henle . This defect leads to reduction in tubular reabsorption of magnesium and produce hypomagnesemia. The reason for this tubular defect in diabetics is not clear. Treatment with insulin has been shown to correct renal loss of magnesium in diabetics. Low dietary intake is an unlikely cause of decreased magnesium status in diabetes. A dietary survey conducted in Germany showed that only >6% of the diabetic group and >19% of the control group had intakes of magnesium below their individual daily requirements. In addition, recently it has been shown that type 2 diabetics in reasonable metabolic control absorb dietary magnesium to a similar extent as healthy controls. Increased urinary magnesium excretion due to hyperglycemia and osmotic diuresis may contribute to hypomagnesemia in diabetes.

Serum levels of magnesium have been found by several investigators to correlate inversely with fasting blood glucose concentration72,73 and the

percentage of HbA1C.72 Schlienger et al.7 studied the influence of glycemic control (glycemic control evaluated by HbA1C) on various trace elements and reported significantly reduced plasma magnesium levels in patients with poor control of diabetes. The present study revealed no statistically significant correlation between serum magnesium levels and fasting blood sugar and HbA1C. However, patients with poor glycemic parameters (FBS>130 mg/dl or 79 HbA1C > 7%) had a significantly higher prevalence of hypomagnesemia (43.4% and 35.8%) compared to over all prevalence in diabetics (31%).

Glycosylated hemoglobin (HbA1C) results from glycosylation of hemoglobin by a reaction between glucose and N-terminal valine of beta chain of Hb molecules. When plasma glucose is consistently elevated, there is an increased glycosylation of hemoglobin. HbA1C assays approximate with mean plasma glucose values over the previous 2 to 3 months. Higher percentages of HbA1C indicate poor glycemic control in the previous months.

Hypomagnesemia is reported to be both a cause and result of poor glycemic control. Magnesium is a cofactor in both glucose transporting mechanisms of cell membrane and various enzymes important in carbohydrate oxidation.4 In addition, magnesium deficiency has been shown to promote insulin resistance in multiple studies. Nadler et al.8 have reported that insulin sensitivity decreases even in nondiabetic individuals after induction of magnesium deficiency. Like wise, elderly subjects were shown to have

improved glucose tolerance when they received magnesium supplements. Thus hypomagnesemia by itself results in poor glycemic control. Conversely, hyperglycemia and osmotic diuresis may lead to increased urinary magnesium excretion and hypomagnesemia in diabetics. However, high prevalence of hypomagnesemia is reported in type – 2 diabetics with good glycemic control.5 So, although poor glycemic control is associated with magnesium deficiency, it is not simply induced by hyperglycemia and is not corrected by improvement in metabolic control alone.

Sex, age and duration of diabetes were not the significant predictors of serum magnesium levels. Yajnick et al.72 in 1984 reported that among diabetics plasma magnesium concentration was directly related to age and men had significantly higher concentrations than women. The increasing magnesium levels with age were probably due to impaired renal function and the sample size was relatively small to confirm male preponderance. In our study, patients with impaired renal functions were excluded. Our results confirm to the recent reports that have not shown any significant associations between sex, age and duration of diabetes with serum magnesium levels.

Significant differences, in serum magnesium concentrations have been reported between the insulin treated and non-insulin treated diabetics. Yajnik et al.72 reported that insulin treated diabetics have significantly lower serum magnesium levels compared to non insulin treated ones. In the present study

prevalence of hypomagnesemia in insulin treated diabetics was higher than in noninsulin treated (32.2% v/s 30.4%). However, the difference was statistically not significant. Walti MK et al have reported that diabetes treatment (insulin or OHA) did not significantly effect hypomagnesemia. Redistribution of magnesium from plasma in to red blood cells is caused by insulin. In a recent study Alzaida et al. have found that cellular uptake of magnesium is normally stimulated by insulin. So insulin treatment may enhance cellular magnesium uptake and result in increased prevalence of hypomagnesemia.

Studies have associated lower serum levels of serum magnesium with higher risk of coronary artery disease. As part of Atherosclerosis risk in communities study, a cohort of 15,792 people were observeseven over 7 years and they found that an increasing relative risk of coronary artery disease with decreasing serum magnesium has been reported.[53]

How a low serum magnesium predisposes to coronary artery diseases is not known. In the present study, no difference in prevalence of hypomagnesemia was found between those with ischemic heart disease and others. Similarly, no difference in prevalence of hypomagnesemia was found between the hypertensive and non hypertensive subjects.

Previously magnesium deficiency has been found to be associated with diabetic microvascular disease. In the present study too significantly higher prevalence low serum magnesiumwas observed in diabetics with microvascular

complications and average serum concentration of magnesium in diabetics with microvascular complications was relatively lower than in diabetics with no microvascular complications and healthy people.

Hypomagnesemia has been reported in patients with diabetic retinopathy, with lower magnesium levels predicting a greater risk of severe diabetic retinopathy. Our observations prompted a definite association between diabetic retinopathy and low serum magnesium levels. There was a significant difference is prevalence of hypomagnesemia in diabetics with retinopathy and without retinopathy (51.3% vs 19%; P< 0.005). These observations are similar to other reports. The mechanism by which hypomagnesemia predisposes to diabetic retinopathy is not clear. Grafton et al. have proposed the inositol transport theory may to explain this association. But the exact reason remains unknown.

With reference to other diabetic microangiopathies, no significant association was found between prevalence of hypomagnesemia, d and diabetic nephropathy. Even within the nephropathy group, no difference was found between patients with microalbuminuria and macroalbuminuria. These results are similar to those reported by Pickup et al. who found no difference in serum magnesium concentrations between diabetics with microalbuminuria or clinical proteinuria compared to diabetics with normal albumin excretion. In contrast, Corsonello, et al demonstrated significantly lower serum magnesium in type 2

diabetics with nephropathy compared to a normoalbuminemic group. They argued that in diabetics with nephropathy, serum magnesium might be reduced because of lower serum albumin concentration, as 30% of serum magnesium is bound to proteins, mainly albumin. In our study, 15 patients had microalbuminuria and 3 patients who had macroalbuminuria had 24 hour albumin excretion less than 1.5 mg. This should not lower plasma albumin, because plasma contains macro-amounts (35-52 g/L) of albumin.

In summary, the present study has demonstrated that hypomagnesemia is common in type 2 diabetics and magnesium deficiency is conclusively associated with diabetic retinopathy. So it may be prudent in clinical practice to periodically monitor plasma magnesium concentrations in diabetic patients. If plasma 83 magnesium is low, an intervention to increase dietary intakes of magnesium may be beneficial.

CONCLUSION

- Prevalence of hypomagnesemia in type 2 diabetics is 30%.
- Prevalence of hypomagnesemia is significantly higher in patients with microvascular diabetic complications compared to diabetics with no complications.
- Hypomagnesemia is significantly associated with diabetic retinopathy.

• No significant association exists between glycemic control, other diabetic microangiopathies (nephropathy and neuropathy) and diabetic comorbidities – ischemic heart disease and hypertension.

SUMMARY

Present study was conducted to estimate the prevalence of hypomagnesaemia in type 2 diabetics and to study the possible association of hypomagnesaemia with diabetic complications like retinopathy and nephropathy .

The study included 100 people with type 2 diabetics, with no factors significantly altering the serum magnesium levels. Fasting serum magnesium levels were taken and correlated with glycemic control and diabetic complications.

The results demonstrated prevalence of hypomagnesaemia in type 2 diabetics as 31% and magnesium deficiency was conclusively associated with diabetic retinopathy. No significant associations were found between serum magnesium levels and other variables – duration of diabetes, glycemic control, mode of diabetic treatment, diabetic nephropathy and hence it is prudent in clinical practice to periodically monitor plasma magnesium concentrations in diabetic patients. If plasma magnesium is low, an intervention to increase

dietary intakes of magnesium rich foods may be beneficial. However, the role of magnesium supplements remains to be evaluated.

ANNEXURE I – PROFORMA

Serial No. :

Patient Details Name :

Hospital No. :

Age:

Sex:

Occupation:

Diabetic History

Age of onset :

Total Duration :

Mode of Treatment

1. Oral hypoglycemic agents : (Suplhanylurea/biguanide)

2. Insulin (Type) :

3. Diabetic Diet :

Symptoms Related to Complications

Symptoms of Nephropathy

• Oliguria :

• Oedema :

Symptoms of Retinopathy

• Dimness of vision : • Blindness :

Past History

• IHD: • HTN:

Family History

• DM: • IHD: • HTN:

Examination

Height: Weight: General Examination: Pulse Rate: Edema:

BP: Supine: Standing:

C. Eye Signs

• Diabetic retionopathy : o Non Proliferative : Proliferative :

D. Signs of nephropathy

• Oedema: • Facial puffiness :

E. Cardiovascular system F. Respiratory system G. Per abdomen

Investigations

1. FBS: PPBS: HbA1C :

2. Serum Magnesium: 3. 24 hour albuminiuria:

4. Urea: Creatinine: 5. Routine Urine: Sugar: Protein: Microscopy:

6 ECG: 7 Others:

DATA ON SERUM MAGNESIUM LEVEL IN TYPE 2 DIABETES AND CORREALTION WITH DIABETIC RETINOPATHY AND NEPHROPATHY

Sl No	Name	Age	Sex	Occu	IP/ OP	DOI	Drugs	Wt (kg)	Ht (m)	BMI	SBP	DBP	FBS	HbA1C	S.Mg	U-Pro	Urea	S.C	LP	NPDR	PR
1	THANGAM	51	F	S	OP	5	OHA	45	1.39	23.29	126	82	141	8	1.6	<300	36	1	N	N	Nil
2	THAYEE	58	F	S	OP	6	OHA	56	1.55	23.31	130	92	136	7	1.6	>300	35	1.1	HL	N	NIL
3	SUSEELA	49	F	NS	OP	3	OHA	78	1.58	31.24	140	80	128	6.5	1.7	<300	35	1	N	N	NIL
4	MEENA	43	F	NS	OP	1	OHA	64	1.62	24.39	126	84	118	6	1.8	<300	28	1.2	HL	N	NIL
5	PANJALI	60	F	S	OP	10	OHA	65	1.57	26.37	156	90	130	8	1.6	>300	36	1.2	HL	P	NIL
6	RANI	57	F	S	OP	9	OHA	75	1.52	32.46	138	90	142	9	1.6	<300	34	1.2	HL	P	NIL
7	KANNAN	65	M	S	OP	8	OHA	76	1.64	29.74	150	100	136	9	1.5	>300	40	1.8	HL	N	NIL
8	GOPAL	65	M	NS	OP	10	OHA+INJ	76	1.58	32.89	140	92	126	7	1.6	<300	36	1	HL	P	NIL
9	JAYARAM	69	M	S	OP	6	OHA	80	1.64	10.02	140	90	132	8	1.6	<300	28	1.1	HL	N	NIL
10	GANGA	61	F	S	OP	5	OHA	65	1.42	32.23	140	90	128	10	1.6	<300	36	1.2	HL	N	NIL
11	AMUDHA	50	F	NS	OP	3	OHA	61	1.6	23.82	130	90	116	7	1.7	<300	36	1.2	N	N	NIL
12	SUNDHARI	74	F	S	OP	12	OHA	60	1.63	22.58	140	90	122	7	1.9	<300	32	1.2	N	N	NIL
13	VIJAYA	42	F	NS	OP	2	OHA	75	1.64	27.81	130	80	126	7	1.8	<300	36	1	N	N	NIL
14	BHAI	45	M	NS	OP	3	OHA	95	1.71	32.49	140	90	132	8	1.8	<300	36	1.2	HL	N	NIL
15	CHANDRA	39	F	NS	OP	1	OHA	50	1.52	21.64	130	80	120	6.5	2	<300	32	1.1	N	N	NIL
16	THAMBI	61	M	S	OP	8	OHA	59	1.65	25.71	126	92	126	9	1.7	<300	36	1	N	P	NIL
17	SURYA	55	F	NS	IP	6	OHA	65	1.7	26.1	122	86	135	10	1.5	>300	36	1.2	N	N	NIL
18	BANU	59	F	NS	OP	8	OHA	67	1.49	30.17	130	82	140	11	1.6	>300	38	1.4	N	N	NIL
19	DURAI	64	M	NS	OP	10	OHA	65	1.42	32.25	140	90	130	12	1.4	>300	36	1.2	HL	N	NIL
20	MANI	52	M	NS	OP	6	OHA	79	1.72	27.33	140	90	136	10.5	1.6	<300	35	1	N	N	NIL
21	RAJENDREN	58	M	NS	OP	8	OHA	62	1.58	24.83	138	92	219	10	1.7	<300	36	1.2	N	N	NIL
22	CHELLAM	75	M	S	OP	10	OHA	56	1.62	21.21	150	90	225	9	1.6	>300	38	1.2	N	P	NIL
23	JANAKI	54	F	NS	OP	4	OHA	66	1.5	29.33	152	90	223	11	1.6	>300	38	1.2	N	P	NIL
24	RUBY	60	F	NS	OP	10	OHA	62	1.6	24.21	100	80	98	6	1.9	<300	32	0.9	N	N	NIL
25	CHANDRA	67	F	NS	OP	6	OHA	68	1.7	28.52	128	90	83	6	1.6	<300	30	1	N	N	NIL
26	MANO	38	M	NS	OP	1	OHA	86	1.65	31.59	130	80	240	9	1.6	<300	29	1.2	N	N	NIL
27	RAJU	64	M	NS	OP	6	OHA	72	1.78	26.37	150	90	180	10	1.6	>300	40	1	N	N	NIL
28	PAKARI	59	M	S	OP	5	OHA	78	1.65	28	150	90	250	11	1.5	<300	42	2.1	N	P	NIL
29	SAMI	64	M	NS	OP	7	OHA	82	1.68	29	138	86	164	9	1.7	<300	30	1.2	N	N	NIL
30	THIRU	50	M	NS	IP	3	OHA	65	1.69	32	140	90	118	7	1.9	<300	30	1.2	N	N	NIL
31	RAMESH	38	M	NS	OP	3	OHA+INJ	68	1.65	23	120	80	148	10	1.5	>300	40	2.5	N	P	NIL

32	PANDU	42	M	NS	OP	5	OHA+INJ	70	1.78	22	120	80	98	6.5	1.8	<300	32	1	N	N	NIL
33	PAVUNU	67	F	S	OP	5	OHA	68	1.53	29.5	140	90	145	11	1.6	>300	36	1.1	N	N	NIL
34	BEEBEE	58	F	NS	OP	8	OHA+INJ	69	1.55	28.72	138	80	185	9	1.6	>300	36	1.2	N	P	NIL
35	USMAN	63	M	NS	OP	11	OHA	72	1.61	27.78	130	80	165	11	1.7	>300	38	1.2	N	P	NIL
36	LATHA	60	F	NS	OP	9	OHA+INJ	69	1.58	27.65	140	90	163	9	1.7	>300	36	1.1	N	N	NIL
37	RANI	50	M	NS	OP	6	OHA	75	1.65	27.55	120	90	154	9	1.8	<300	32	1	N	N	NIL
38	MANJULA	49	F	NS	OP	3	OHA	64	1.75	20.09	120	80	100	11	1.6	<300	30	1	N	N	NIL
39	RAMAN	61	M	NS	IP	10	OHA	73	1.71	24.96	136	92	168	10	1.7	>300	38	1.2	HL	P	NIL
40	BALA	57	M	NS	OP	6	OHA	75	1.78	23.67	128	96	115	6	1.8	<300	32	1.2	N	N	NIL
41	MOHAN	56	M	NS	OP	6	OHA	75	1.48	34.24	130	80	263	11	1.6	>300	36	1.2	HL	P	NIL
42	KAMALA	45	F	NS	OP	5	OHA	68	1.63	25.59	134	83	111	9	1.8	<300	34	1	HL	N	NIL
43	KASTHURI	48	F	NS	OP	3	OHA	70	1.56	28.76	130	80	144	9	1.7	>300	36	1.6	HL	N	NIL
44	SUMAN	69	M	NS	OP	11	OHA	69	1.56	27.99	110	82	121	8	1.8	<300	32	1.2	N	N	NIL
45	KATTAN	52	M	NS	OP	6	OHA&INJ	78	1.58	34.67	110	78	148	9	1.6	>300	36	1.2	HL	N	NIL
46	PICHAI	70	M	S	OP	10	OHA	70	1.69	24.51	148	82	105	6	1.7	<300	32	1	N	N	NIL
47	NEELA	71	F	S	OP	9	OHA	65	1.55	27.06	136	88	128	7.5	2	<300	36	1	N	P	NIL
48	THULASI	48	F	NS	OP	5	OHA	64	1.67	22.95	140	78	132	8	1.9	<300	34	1.1	N	N	NIL
49	ARUMUGAM	50	M	NS	IP	5	OHA&INJ	76	1.69	26.61	130	82	152	9	1.7	>300	36	1.2	HL	NI	NIL
50	MURUGAN	48	M	NS	OP	4	OHA	85	1.71	29.07	140	94	252	9.5	1.6	<300	35	1.1	HL	P	NIL
51	KRISHNAN	55	M	NS	OP	5	OHA	80	1.75	26.12	132	82	152	10	1.9	<300	33	1	N	N	NIL
52	BABU	38	M	NS	OP	1	OHA	79	1.8	24.38	128	88	150	8.5	1.9	<300	34	1.1	N	N	NIL
53	THAYALAN	39	M	NS	OP	1	OHA	70	1.74	23.12	124	80	126	8	1.7	<300	36	1	N	N	NIL
54	KALA	40	F	NS	OP	4	OHA	64	1.61	24.69	110	86	105	6.5	1.9	<300	34	1.1	N	N	NIL
55	MURTHY	54	M	NS	OP	8	OHA	73	1.78	23.04	112	82	121	7	1.6	>300	30	1.2	N	N	NIL
56	SASIKALA	41	F	NS	OP	1	OHA	65	1.63	24.4	140	90	115	8	2	<300	36	1.1	N	N	NIL
57	MUTHU	58	M	NS	OP	7	OHA	74	1.74	24.1	130	80	110	6	2	<300	35	1	N	N	NIL
58	RAJA	54	M	NS	IP	4	OHA	72	1.69	25.21	140	82	148	10	1.6	>300	40	1.8	HL	P	NIL
59	SELVAM	52	M	NS	OP	3	OHA	83	1.84	24.52	110	82	96	6	2.1	<300	36	1.1	N	N	NIL
60	SHEELA	58	F	NS	OP	8	OHA&INJ	58	1.5	25.78	120	90	92	6	2	<300	34	1	N	N	NIL
61	JAMEELA	52	F	NS	OP	6	OHA	100	1.55	41.62	140	90	223	10	1.6	>300	36	1.2	N	N	NIL
62	RUPA	49	F	NS	OP	9	OHA+INJ	95	1.65	34.89	140	90	245	10	1.6	>300	40	2	HL	P	NIL
63	ELLAMMAL	63	F	S	OP	9	OHA	65	1.51	28.51	140	80	189	10	1.6	>300	36	1	N	N	NIL
64	THIYAGU	70	M	S	OP	10	OHA	67	1.76	21.63	150	90	90	6.5	1.8	<300	28	1.2	N	N	NIL
65	KILLIAMMAL	69	F	S	OP	9	OHA+INJ	64	1.6	25	150	90	98	6	1.8	<300	28	1.2	N	N	NIL
66	NADHU	41	M	NS	OP	6	OHA	72	1.75	23.51	30	80	116	6.7	1.7	<300	32	1	N	N	NIL

67	PUSHA	59	F	NS	OP	6	OHA+INJ	69	1.57	27.99	150	90	320	11	1.5	>300	36	1.2	N	N	NIL
68	MURALI	51	M	NS	OP	5	OHA	69	1.69	24.16	140	90	236	10	1.7	>300	30	0.9	N	P	NIL
69	LAKSHMI	59	F	NS	OP	6	OHA+INJ	69	1.57	27.99	150	90	220	11	1.6	>300	38	1.2	N	P	NIL
70	SUNDHARI	61	F	S	OP	10	OHA	70	1.55	29.14	140	80	200	11	1.6	>300	30	1.7	N	N	NIL
71	MUNIAMMAL	65	F	S	IP	12	OHA	75	1.52	32.46	130	90	187	9	1.6	<300	26	1	N	N	Nil
72	VARADHAN	75	M	S	OP	15	OHA&INJ	69	1.68	24.45	140	90	210	9	1.6	>300	36	1.2	N	NI	NIL
73	SARASU	68	F	NS	OP	10	OHA	65	1.76	20.98	120	86	188	8	1.6	>300	36	1.2	N	P	NIL
74	MANIMEGALAI	67	F	NS	OP	7	OHA	62	1.58	24.84	150	90	200	11	1.5	>300	36	1.2	N	P	NIL
75	URLAMILA	48	F	NS	OP	5	OHA	68	1.6	26.54	140	90	135	7	1.8	<300	30.8	1.2	HL	P	NIL
76	BRINTHA	40	F	NS	OP	2	OHA+INJ	65	1.65	23.88	130	80	98	6	2	<300	32	1	N	N	NIL
77	BANU	39	F	NS	OP	1	OHA	60	1.62	22.86	130	90	90	6.5	2	<300	26	1	N	N	NIL
78	MEERA	45	F	NS	OP	3	OHA	65	1.59	22.79	126	86	101	7	1.7	<300	28	0.8	N	N	NIL
79	JAYATHI	40	F	NS	OP	2	OHA	60	1.63	22.58	128	78	93	6.5	2	<300	30	1	N	N	NIL
80	KAMATCHI	58	F	S	IP	5	OHA	70	1.66	25.4	130	90	98	6	1.6	<300	32	1	N	N	NIL
81	POOGKODI	55	F	NS	OP	3	OHA	65	1.59	25.71	128	78	105	7	2	<300	28	1	N	N	NIL
82	AMMU	45	F	NS	OP	2	OHA	66	1.58	26.44	126	82	110	8	2	<300	27	1	N	N	NIL
83	SURYA	52	M	NS	OP	6	OHA&INJ	68	1.52	29.43	136	88	112	8	1.7	>300	36	1.2	HL	P	NIL
84	VEERAN	72	M	S	OP	10	OHA	65	1.71	22.23	148	88	115	8.5	1.7	<300	37	1.2	N	N	NIL
85	RATHINAM	78	M	S	OP	12	OHA	78	1.65	25.86	146	90	105	7	1.7	<300	36	1.2	N	N	NIL
86	GOMATHI	69	F	S	OP	12	OHA	65	1.54	27.41	150	100	185	10	1.6	>300	36	1.2	N	P	NIL
87	SEETHA	65	F	S	OP	9	OHA	59	1.59	23.34	148	90	122	7	1.8	<300	30	1.2	N	N	NIL
88	MANI	41	M	NS	IP	1	OHA	75	1.72	22.35	120	8	110	77	1.7	<300	34	1	N	N	NIL
89	SRINIVAS	40	M	NS	OP	1	OHA	70	1.65	25.71	116	78	126	8	1.9	>300	32	1	HL	N	NIL
90	MOHAN RAJ	52	M	NS	OP	4	OHA	65	1.66	23.79	126	70	114	7	1.6	<300	32	1	N	N	NIL
91	DHANAM	55	M	NS	OP	5	OHA	56	1.67	20.08	130	80	96	6.5	2	<300	36	1.2	N	N	NIL
92	THIRUPATHI	60	M	NS	OP	6	OHA	58	1.6	23.39	150	90	89	6.6	2	<300	28	1	N	N	NIL
93	ARUL	42	M	NS	OP	3	OHA	65	1.71	25.97	140	80	100	7	1.9	<300	28	0.9	N	N	NIL
94	NARESH	48	M	NS	OP	5	OHA&INJ	70	1.73	27.6	136	80	109	7	1.8	<300	34	0.8	N	N	NIL
95	DILLI RANI	63	F	S	OP	10	OHA	60	1.52	29.22	140	90	96	7	1.6	<300	36	0.7	N	N	NIL
96	SIVAGAMI	65	F	S	OP	10	OHA	65	1.55	26.3	150	100	256	7	1.8	<300	39	1	N	N	NIL
97	ANJALI	67	F	S	IP	10	OHA	64	1.48	25.39	140	96	101	6	1.9	<300	31	1.2	N	N	NIL
98	SURESH	48	M	NS	OP	5	OHA&INJ	64	1.56	26.3	130	80	156	6	2	<300	30	1.1	N	N	NIL
99	MALAR	58	F	NS	OP	8	OHA	65	1.6	25.39	128	86	181	6.4	1.8	<300	28	0.9	N	N	NIL
100	KUMAR	52	M	NS	OP	5	OHA	73	1.68	25.86	148	90	108	6.4	1.9	<300	30	1	N	N	NIL
101	LEELA	55	F	NS	OP	4	OHA	67	1.54	28.25	130	84	121	7	1.7	>300	36		N	N	NIL
102	SHANMUGAM	59	M	NS	OP	7	OHA	72	1.63	27.1	128	80	111	6.5	1.8	<300	32		N	N	NIL
103	RAVI	69	M	S	OP	9	OHA	70	1.64	26.03	140	86	138	9	1.9	<300	34		N	N	NIL
104	MANNU	66	M	NS	OP	7	OHA	67	1.7	23.18	138	90	120	7	2	<300	30		N	N	NIL
105	SIVA	45	M	NS	OP	3	OHA	79	1.71	27.02	140	90	118	7	2	<300	32		N	N	NIL
106	RAMU	56	M	NS	OP	4	OHA	60	1.68	21.26	146	98	100	6.5	1.9	<300	31		N	N	NIL
107	VADAMALAI	69	M	S	OP	11	OHA	69	1.74	22.79	120	82	132	8	1.7	>300	32		HL	P	NIL
108	DHAMU	56	M	NS	IP	3	OHA	73	1.58	29.24	130	80	125	7.5	1.9	<300	34		N	N	NIL

ANNEXURE III

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